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CIMBURA(2)

ROYAL COMMISSION OF INQUIRY INTO CERTAIN
DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND
RELATED MATTERS.

Hearing held
8th floor
180 Dundas Street West
Toronto, Ontario

In Ch. P. H. C.
X Beam
Forster.

The Honourable Mr. Justice S.G.M. Grange

P.S.A. Lamek, Q.C.

E.A. Cronk

Thomas Millar

Commissioner

Counsel

Associate Counsel

Administrator

Transcript of evidence
for

October 19, 1983

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ROYAL COMMISSION OF INQUIRY INTO CERTAIN
DEATHS AT THE HOSPITAL FOR SICK CHILDREN
AND RELATED MATTERS.

Hearing held on the 8th Floor,
180 Dundas Street West, Toronto,
Ontario, on Wednesday, the 19th
day of October, 1983.

- - - - -

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner
THOMAS MILLAR - Administrator
MURRAY R. ELLIOT - Registrar

APPEARANCES:

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D. HUNT)	Counsel for the Attorney
L. CECCHETTO)	General and Solicitor General
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	and Coroner's Office)
I.G. SCOTT, Q.C.)	Counsel for The Hospital
I.J. ROLAND)	for Sick Children
D. YOUNG	Counsel for The Metropolitan
	Toronto Police
K. CHOWN	Counsel for numerous Doctors
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	Children
F. KITELY	Counsel for the Registered
	Nurses' Association of Ontario
	and 35 Registered Nurses at
	The Hospital for Sick Children

(Cont'd)



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G.R. STRATHY) E. FORSTER)	Counsel for Phyllis Trayner - Nurse
J.A. OLAH	Counsel for Janet Brownless - R.N.A.
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F.J. SHANAHAN	Counsel for Mr. & Mrs. Dominic Lombardo (parents of deceased child Stephanie Lombardo); and Heather Dawson (mother of deceased child Amber Dawson)
W.W. TOBIAS	Counsel for Mr. & Mrs. Hines (parents of deceased child Jordan Hines)
J. SHINEHOFT	Counsel for Lorie Pacsai and Kevin Garnett (parents of deceased child Kevin Pacsai).



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--- Upon commencing at 10:00 a.m.

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THE COMMISSIONER: Yes, Mr. Hunt?

4

MR. HUNT: I wonder, Mr. Commissioner,

5

before we start this morning if I could just make one

6

comment. We still have before us the question of

7

Dr. Soldin's request for samples which he made the

8

day before yesterday, and having had an opportunity --

9

MR. LAMEK: Excuse me, Mr. Commissioner,

10

I wonder if Mr. Hunt could go to a microphone. The
reporter can't hear him and I doubt that anyone else

11

can.

12

THE COMMISSIONER: All right.

13

MR. HUNT: Yes, sir. As I indicated

14

we still have before us this request. Now the

15

inventory of the samples that are available will be

16

completed today at the Centre for Forensic Sciences,

17

and it will be available I expect some time before

18

Mr. Cimbura finishes testifying, and then we will at

19

Now after reviewing the transcripts

20

of Dr. Soldin's evidence I would like to make our

21

submission very clear with respect to this.

22

Firstly, we have no objection whatsoever

23

to some appropriate person or body testing the samples

24

that are still available, assuming that they are in

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A.2

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2 a satisfactory condition to be of some assistance to
3 us. But in light of some of the evidence given by
4 Dr. Soldin I can indicate in my submission it raises
5 really serious concern as to whether or not the
6 samples ought to be turned over to him in compliance
7 with his request at this particular time.

8 Firstly, I suggest there is no
9 question whatsoever but that his project is clearly
10 in the experimental stage; it is a research project,
11 and he is nowhere near ready to use these samples to
12 provide us with the definitive results that he seemed
13 to suggest that he could provide us with when he made
14 his comment to the Commission on Tuesday. And in
15 light of the fact that we are certainly limited in
16 respect of what we have, in my submission it would
17 be inappropriate to turn whatever samples there are
18 over to Dr. Soldin or anybody whose interest in them
19 is clearly one of a research nature to further their
20 own research into the subject.

21 If anybody is to get them for testing
22 in my submission it should be only after a very careful
23 assessment of the capabilities of whomever it is in
24 terms of the state of their methodology, and that
25 should be done I think with all of the interested
parties having an opportunity to explore it.



A.3

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2 Secondly, and it is with regret that
3 I suggest that there is concern raised by some of
4 Dr. Soldin's questions with respect to his objectivity
5 in this whole matter.

6 In my submission he did not appear to
7 be the objective scientist who is interested in these
8 materials for their scientific value solely, but he
9 seemed to indicate that he held some views with
10 respect to the inappropriateness of how the samples
11 had been dealt with at this point and suggested indeed
12 that there was some bias being shown against his
13 laboratory in terms of caution that was being urged,
14 and in my submission that raises a concern with respect
15 to Dr. Soldin's objectivity in this matter.

16 It may be that at some point in time,
17 if his project has gone beyond the research stage
18 and he can return and satisfy the Commission of the
19 state of his methodology, and perhaps the excitement
20 of the present situation with his research which is
21 ongoing has turned into scientific fact, it may be
22 that he would be the appropriate person to release
23 them to, but at this point in time in my submission
24 he would not be so.

25 THE COMMISSIONER: Yes. Before hearing
from anyone else would it not be reasonable to wait



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for a formal request from counsel - I don't take Dr. Soldin's request as meaning anything at the moment. I think when that request comes from Mr. Scott or from someone else we will then deal with it. Wouldn't that be --

MR. HUNT: That would certainly be satisfactory as far as I am concerned.

THE COMMISSIONER: Do you have any objection to that, Mr. Scott?

MR. SCOTT: I would like to respond.

THE COMMISSIONER: Yes, but not for my purposes but for whatever other purposes, by all means respond to it, but in the course of your response would you help me out?

MR. SCOTT: My responses are always directed to assist you and your purposes, Mr. Commissioner.

Let me say that the evidence of Dr. Soldin is before you, and the request that he has made is there. I think it is worthwhile to remember that we are engaged here in both what may amount to a forensic murder case or what may amount to a scientific examination about the impact of digoxin or other substances in the body, and the Commission is going to have to consider both of those aspects of its work.



A.5

1
2 Now Dr. Soldin is not only a staff
3 member of the Hospital, he is a member of the
4 university staff and is a Professor in the Department
5 of Biochemistry at the University of Toronto and the
6 Hospital is of course a university as well as a
7 hospital in the practical sense.

8 I want to begin by saying that I am
9 offended by the first suggestion made by the Attorney
10 General that the studies are at a preliminary stage.
11 Of course they are at a preliminary stage, and they
12 can't be carried forward unless examination of the
13 appropriate materials is permitted.

14 They will never be at a final stage
15 until these kinds of examinations can be done, and
16 therefore I look in the long term to co-operation
17 from the Attorney General's Department in permitting,
18 if it be considered appropriate, to have those studies
19 done.

20 The way to achieve that it seems to
21 me is to permit the witness to get together with
22 Mr. Cimbura to say what he would like to do, and to
23 see if that can be done in a way that is not damaging
24 to the material and will advance the science. And
25 I will play some part in seeing to it that they
get together for the purposes of determining if these



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tests can be done and when they can be appropriately done.

For the Attorney General to say that he doesn't think much is going to come of them is of course a highly unscientific observation, quite unwarranted.

THE COMMISSIONER: Not much will come of it right now. That was all he was saying.

MR. SCOTT: Well --

THE COMMISSIONER: He wasn't saying it wouldn't come of it.

MR. SCOTT: Well, he went further than that.

Mr. Hunt made an attack yesterday on the witness by asserting that he was doing his tests in essence for some ulterior purpose.

Now he can suggest whatever he wants in cross-examination: that is his affair and he answers within his Department to the questions he puts.

The witness got angry at that, as one might well expect. It is in my respectful submission an unusual remark to be made by counsel.

Now we have Mr. Hunt suggesting without any basis whatever, and most unfairly in the face of the public press, that the witness is not objective,



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2 and in my submission I would anticipate that this
3 morning Mr. Hunt will be good enough, unless he has
4 clear evidence that that is the case, and remembering
5 that he is speaking of a senior staff member of the
6 Hospital and a senior professor at the university, to
7 withdraw that observation.

8 That isn't to say that he can't make
9 submissions about the witnesses and the impact of
10 their evidence in the end, but I wouldn't have thought
11 that the Attorney General's Department wants at this
12 early stage that observation that a senior respected
13 scientist is not objective to remain on the public
14 record, and I look forward to Mr. Hunt withdrawing it.
15 For which purpose I cede the microphone, as they say
16 in the Senate of the United States.

17 THE COMMISSIONER: It is not necessary
18 to reply to that, Mr. Hunt. If anybody insists on
19 making further application they may, but I do not see
20 yet a formal application for these samples to be
21 made available to anyone.

22 Mr. Lamek, can you presumably take
23 charge of the problem?

24 MR. LAMEK: Yes, I will gladly do that,
25 Mr. Commissioner. If anyone approaches me with such
a request I will bring it to your attention.



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THE COMMISSIONER: Well I think there has been a request, though, that Mr. Cimbura and Dr. Soldin might get together. You might do what you can to promote that cause.

MR. LAMEK: I will be glad to do that.

MR. SCOTT: Well, we will see that that is done as well.

I must say for the purposes of the press who are here I am gravely offended by that observation. I don't think the suggestion of Mr. Hunt has been made of any other witness in this Inquiry to date and I think it is a most unfortunate precedent; extremely damaging if not borne out.

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/DM/ak

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3 THE COMMISSIONER: Well, I indicated
4 in the first instance that for my benefit it wasn't
5 necessary to make that observation but you have made
6 it. Now, can we get on with the matter at hand.

7 MR. LAMEK: Mr. Commissioner, we
8 have this morning what I call the second coming of
9 Mr. Cimbura.

10 THE COMMISSIONER: All right.

11 MR. LAMEK: May I have Mr. Cimbura
12 please in the witness box. By all means sit down,
13 Mr. Cimbura.

14 GEORGE CIMBURA, Recalled

15 THE COMMISSIONER: You have been
16 sworn, Mr. Cimbura, so that it is not necessary again.

17 THE WITNESS: Thank you.

18 DIRECT EXAMINATION BY MR. LAMEK:

19 Q. We have less spacious surround-
20 ings for you this time, Mr. Cimbura, than we had last
21 time and I am sorry.

22 Mr. Cimbura, I want to cover three
23 areas with you today if I may.

24 First to go into some of the information
25 that you agreed to provide when you gave your evidence
on your methodology back in June.

Second, I want to refer with you to



1
2
3 the results of your analys~~e~~s of the various samples
4 from children who died at the Hospital for Sick
5 Children, the samples that you received and assayed.

6 And then third I want to discuss with
7 you certain other research studies that you have made
8 into matters bearing on the digoxin assay results
9 that you and the Hospital for Sick Children did in
10 this matter.

11 It may be useful at the outset,
12 Mr. Cimbura, to remind ourselves very briefly of
13 the methodology that you described to us at some
14 considerable length last time you were here. Let
15 me be sure that I have it right and if I don't you
16 tell me.

17 In the first place in terms of prepara-
18 tion of the sample you have told us that in your
19 methodology in the case of a tissue sample, you
20 first cut and weigh and homogenize it; do I have
21 that correct?

22 A. That is correct.

23 Q. You turn it into a more or
24 less liquified form of, ideally, uniform quality and
25 character I take it?

A. That is correct.

Q. Then with respect to both



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blood and tissue, your methodology calls for the performance of an extraction process, does it not?

A. That is correct.

Q. And that is done with an organic solvent, and it is designed as I understood you, to purify this sample, to remove some of the elements from the gross sample with which you have no concern and which may interfere with the assay?

A. That is correct.

Q. Now, in that extraction process, you have told us some digoxin is lost from the sample but your studies disclosed that you recovered on the average about 85 per cent of the digoxin that was originally in the sample and we will come to some of those studies this morning.

A. Okay.

Q. You then conducted the RIA on that extracted sample, and you explained your modifications of the RIA procedure, or the particular procedure that you adopted. It is as I understand it what is called a double antibody procedure. That is to say you use the antibody in the normal way to collect the digoxin, and then you use an antibody as a sort of filtration device to assist the collection of the complexes of antibody and digoxin



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molecules; do I have that correct?

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A. In a sense, yes.

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Q. From approximately the late

5

summer of 1981 you were able to use the HPLC procedure

6

in conjunction with the RIA, were you not?

7

A. Yes, late summer or early fall,
yes, something like that.

8

Q. And we will see^{on} which samples

9

later; but with many samples, as I understood you,

10

having done the RIA on the sample, you then ran the

11

sample through the HPLC with a view to eliminating

12

digoxin metabolites and certain other substances

13

which might react with the antibody in the RIA, and

14

then you ran that separated sample through RIA again,

15

you did that with many of the samples that were sent
to you, did you not?

16

A. That is correct. In addition

17

to that we have run quite often a third RIA just

18

before the HPLC separation. So that very often we

19

ran actually three RIA's, one to start with, one

20

before the HPLC and one after the HPLC.

21

Q. That was by way of a brief

22

review so we can ^{all} ~~always~~ remind ourselves of what it
is that you were doing in your laboratory,

23

Mr. Cimbura.

24

Now, when you were originally giving

25

evidence back in June, early July, certain counsel



1
2 and in particular Mr. Scott for the Hospital, asked
3 you to provide certain information about details of
4 your analytical method, or about matters going to
5 the reliability of your method and the results, do
6 you recall that?

7 A. Yes, some of it, yes.

8 Q. Now I understand that to the
9 extent that it was available to you you have reviewed
10 the information in your file and you ^{have} prepared summaries
of it?

11 A. That is correct.

12 MR. LAMEK: Now those, Mr. Commissioner,
13 have been distributed.

14 I will ask Mr. Cimbura whether
15 the bundles which have been distributed are indeed
16 the tabular summaries that he has prepared, and if
17 so I will ask that the bundle be marked as the next
exhibit, please.

18 THE COMMISSIONER: Yes. Summaries
19 of what, how are we describing them.

20 MR. LAMEK: Q. Summaries of studies and
21 what shall we call this: research projects, Mr. Cimbura?

22 A. Experiments, research projects,
23 yes.

24 Q. Have I correctly described the
25



1
2 bundle I have given to you, Mr. Cimbura?

3 A. Yes, I recognize them all.

4 If I may add, Mr. Lamek, when you are
5 talking about a brief description of the methodology,
6 I believe I also mentioned in some instances we used
7 gas chromatography and mass spectrometry in some
8 instances.

9 Q. Yes and I will come to those
10 when we look at the results, Mr. Cimbura.

11 Might this bundle be the next exhibit,
12 Mr. Commissioner?

13 THE COMMISSIONER: Yes, all right,
14 Exhibit 213.

15 ---EXHIBIT NO. 213: Bundle of Experiments and
16 Research Projects

17 MR. LAMEK: Q. Now, Mr. Cimbura,
18 let me be clear: for the purposes of my examination
19 I don't propose to take you to the underlying detailed
20 information in your files on the basis on which these
21 summaries were prepared. I understand that informa-
22 tion is available and if it should be important and
23 relevant that you either refer to it or produce it,
24 it can be done I understand?

25 A. That is correct.



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Q. Now you were asked by Mr. Scott about recovery studies that had been conducted, I take it in the course of establishing the procedure for your radioimmunoassay for digoxin; do you recall that?

A. Yes.

Q. Now the first document in the bundle, Mr. Cimbura is headed: "RIA Overall Recovery Blood (Low Concentrations)".

Now you were good enough to have slides and transparencies made of these very documents. Unhappily the lighting conditions don't lend themselves to the legibility of those, but happily we all have a piece of paper in front of us.

Would you explain to me, please, just what this document reports?

A. Yes. First of all I would like to just comment on my ^{ology}termination of "Low Concentrations" there.

Q. Yes.

A. Because certainly 25 nanograms per millilitre is not a low concentration in the sense of its pharmacological effect, but I used this term to express relativity to higher concentrations that I have also studied later on.



1
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3 This particular experiment was carried
4 out, as I recall, it ^{was} early in our evaluation in the
5 period of evaluation of various methodologies that we
6 were evaluating and before we started to apply these
methodologies to the case material.

7 The purpose was at that time to study
8 the recovery rate and also get an idea of the
9 variations between the results as we obtained them.

10 Q. If I understand it correctly,
11 in the left hand column: "Target concentrations"
12 expressed in "Nanograms per Millilitre", those are
13 the known concentrations in the samples that you
assayed, is that so?

14 A. That is right. These are
15 the concentrations, these were our targets, that is
16 what we hoped to achieve by adding known quantities
17 of digoxin to samples of outdated Red Cross whole
18 blood.
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Q All right. Let's take the second line where you had 2 nanograms per millilitre. I take it you spiked the blood with that concentration of digoxin, ran through the assay procedure to see how much of it in fact you got back?

A That's right, it was spiked to produce the concentration.

Q Yes.

A And then the blood was subjected for each concentration to three complete analyses and at the end of these analyses we determined what the measured concentrations were.

Q All right. And that takes us *through* to the first three columns of numbers reading from the left, does it not?

A That is right.

Q That is to say, a target concentration of 0.5, you recorded as recovering nothing, but that I take it is because your calibration scale didn't go down that low?

A That's right. Our detection limit is usually about 1 nanogram per millilitre. So that this is the expected result that would show as negative with the spiked concentration of 0.5 nanograms per millilitre.



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Q And in performing the assay procedure on these samples, I take it you went through the extraction process, the whole procedure that would apply in your assay in the usual course?

A That is right, yes.

Q And at a level of 2 nanograms per millilitre you recovered 1.6 on your measurement, that is to say, 84.3 per cent of the known digoxin in the sample?

A That is correct, sir.

Q And so the numbers read down. There is a significant drop off from 84.2 and 3 to 64.7 when you get to the level of 25. Is there any explanation for that that you are aware of, Mr. Cimbura?

A Well, I have reviewed the analytical analyses and they were all correct as far as I could determine. It is lower than the others. The only possible explanation I can have is that this was at the preliminary stages of our procedure before it was applied to the actual case samples.

Q All right.

A And perhaps we didn't have as much experience but I really cannot see any analytical error when I reviewed the findings.

Q Well, we will see a recovery



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rate on that concentration in a moment again. Could you explain for us please the final column, the intra-assay precision expressed in CV per cent. I understand that means coefficient of variation expressed as a per cent?

A. That is correct, sir. A CV per cent stands for coefficient of variation in per cent.

Q. What does that mean, please?

A. This is a statistical measure quite commonly used in scientific measurements to express the extent of variations between different results obtained. The reason for doing these is that quite usually by any analytical procedures you would not expect to get identical results, there are always variations.

Q. Yes.

A. And the purpose of studying the CV per cent is to assess the extent of these variations.

Q. And as expressed on the document at which we are looking now, Mr. Cimbura, CV per cents of 2.3, 4 and 6.8, are those in your experience and your opinion as a toxicologist acceptable degrees of variation?

A. Yes.



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Q Now, the second document in the bundle, Mr. Cimbura, is a similar summary, but here with respect to blood with high concentrations of digoxin?

A That is correct.

Q Beginning at 25 and going up to 150. Can you give me an idea when in relation to the first study this second study was performed?

A I have the exact date available should it be required. I don't recall it but it was later on.

Q It was later on?

A It was later on, Yes.

Q And again the same technique went into this summary that is summarized on this second sheet, did it?

A That is correct, sir.

Q And there the recovery rates ranged, as it says, from 81.4 up to 86.9.

A That is correct, sir.

Q Averaging over those five levels of concentration 84.1.

A That is correct, sir.

Q I think you told Mr. Scott that your recollection was that your average recovery rate



C.5

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2 was in the order of 85?

3 A. As I recall it that is the
4 average I used but I had difficulty because of the
5 various types of experiments that we have done.

6 Q. Of course.

7 A. And as a matter of fact I haven't
8 had an occasion to adapt all these variations and to
9 see how my estimate at that time comes to exactly.

10 Q. And the intraassay precision
11 expressed as coefficient of variation percentage
12 listed also, and again you regard that degree of
13 variation as being within acceptable scientific limits?

14 A. Yes, I regard it very adequate
15 for forensic toxicological work, yes.

16 Q. Thank you. The third document
17 is again a summary of a recovery study, this time with
18 blood with extreme concentrations of digoxin, that is
19 to say, three levels of concentration: 100, 200 and
20 400 nanaograms per millilitre. The study I take it
21 ~~is~~ ^{was} conducted in the same way as you have described
22 for us?

23 A. Yes. One additional point here
24 is that I have made a note here that in this experiment
25 it involves four complete analyses of individually



C.6

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prepared spiked samples. I think the point that I would make is that for each of these concentrations there were four separate spikings.

5

Q. I see. You didn't spike one big sample with, let us say, up to 100 nanograms and then subdivide that into four for assay?

6

7

A. We did not, that's right.

8

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Q. You took four separate samples spiking each?

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A. That is correct, yes.

11

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Q. For a concentration of 100. What is the significance of that?

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A. Well, the significance of that, when I studied, when I see the results is that the interassay that was done in two different assays so that the CV per cent is expressed as inter rather than intra assay.

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Q. I see, yes.

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A. And when I looked at the results the variations are somewhat greater than before and the information I just provided may be partially responsible for these operations.

21

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Q. Are you suggesting that the spiking may not be uniform to each sample?

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A. Well, there is always a possibility



C.7

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2 in that, yes, that is right. To spike a sample you
3 have to go through certain steps, quite a few steps,
4 and there is always a possibility that this will
5 increase to some extent the error than if you, as you
6 said, spike one sample and you just divide it into
7 four portions.

8 Q Mr. Cimbura, it is clear that
9 at least with respect to the concentrations of 200 and
10 400 nanograms per millilitre your recovery percentage
11 is quite substantially lower than at the lower levels
12 of concentration that we have seen?

13 A That's right.

14 Q You regard those recovery rates
15 as nonetheless satisfactory for the purposes upon
16 which you were engaged?

17 A Yes, for the purpose that I am
18 engaged I think they are adequate, that's right.

19 Q And would you regard it as
20 appropriate if you are recovering 60 or 70 per cent
21 of the digoxin in the sample to apply a correction
22 to the result to compensate for that loss of digoxin?

23 A Well, I would prefer not to use
24 a correction factor, that way I am sure that my
25 results are at least minimal and that perhaps by using
an inappropriate correction factor I don't elevate



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the results more than they actually are.

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Q All right. And then the fourth one in the bundle, Mr. Cimbura, again a summary of a recovery study, this time with respect to liver tissue. Now, I ask you first why liver tissue? What is the significance of liver tissue as opposed to any other kind of tissue?

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A Well, this experiment was done, as I recall it, about the time where we have received a group of exhumed children for examination.

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Q Yes.

A And liver tissue was present in some of them. Another reason, as I recall it, I had in designing this was that liver tissue from an analytical toxicological point of view is usually more difficult to analyze because of the relatively greater amount of impurities that you have from liver tissue let's say than from other organs.

18

19

20

Q All right. Are you suggesting that if you can successfully analyze liver tissue that other tissues are relatively easier?

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A Well, from that point that I mentioned.

Q Yes.

A From the point of view that I mentioned.

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Q. The study is divided into two parts, A and B, each of which deals with two known concentrations I take it, 100 and 300 nanograms per gram?

A. That is correct, sir.

Q. And A, as I understand the note, sets out the results after subjecting the sample to one extraction process?

A. That is correct, sir.

Q. Whereas B, the samples were subjected to two extraction processes before the RIA?

A. That is correct, sir.

Q. What was the purpose of doing two extraction processes?

A. The purpose was to give us an idea what - normally one would expect each time you extract you lose a little bit more, and to give us an idea how much more is lost when you use a second extraction which in some of the samples was necessary because of the purification that was required of the samples.

Q. That accounts for the lower recovery rate in the B part of the study than in the A part of the study?



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2

A. That is right. That is exactly what I expected, the decrease there because I didn't know the numbers.

3

4

Q. Each time you go through the extraction you are going to lose a little more of your material?

5

6

A. That is correct, sir.

7

8

Q. In fact, Mr. Cimbura, in conducting the tissue analyses at the Centre for Forensic Sciences did your procedure call for one or two extraction processes?

9

10

11

A. As I recall them and we did an analysis on many items, but as I recall it whenever it was possible we did it at least in duplicate, at least for each sample two complete extractions.

12

13

14

Q. And again there is the column of intraassay precision, and I take it in light of what you have already told me that that level of variation within the assay was acceptable for your purposes?

15

16

A. That is right. Very good. Very good level.

17

18

Q. You were pleased with that one?

19

A. Yes.

20

Q. All right.

21

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25



1
2 Now do those four documents, Mr.
3 Cimbura, summarize the recovery rate studies that
4 were done in your lab?

5 A. There was additional study
6 that we scheduled recently.

7 Q. Right.

8 A. That I didn't have an
9 opportunity because when I was told before the
10 Commission to put together ---

11 Q. Yes.

12 A. One additional one that I
13 know of that was done in a period before we started
14 to apply our procedure to case samples, and in a
15 sense this used attritiated digoxin to study the
16 recovery rate.

17 Q. What is attritiated digoxin,
18 please?

19 A. Well, attritiated is digoxin
20 with labelled radioactivity. It has incorporated
21 a known amount of radioactivity, and you can study
22 a recovery rate by using - by counting what radio-
23 activity you get at the end of the experiment.
24 You know how much you begin with and we can count
25 the radioactivity at the end.

Q. Do I understand that you



1
2 didn't have time to prepare a summary of that study
3 comparable to the one we have looked at? Do you
4 have any recollection of the recovery rate you were
5 obtaining on that study?

6 A. Well, I haven't had an
7 occasion to examine all the details, but my impression
8 is around 75% at that time. We have done that -
9 that was done in many parts, but my impression is
about 75%.

10 Q. Okay. Now Mr. Scott also
11 asked you about something he called a between day
12 precision study, and at the time you remember that
13 was a matter of some confusion but I think misunder-
14 standing between you. That was not a term with which
you were particularly familiar.

15 We have looked at some intra and inter
16 assay precision studies as part of the first four
17 documents.

18 The next document is headed RIA
19 Interassay Precision, and can you tell me what was
20 the purpose of this study?

21 A. Well, I suppose the ultimate
22 purpose of this document was to answer some questions
that I was ---

23 Q. Yes, but what was the purpose
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of the study that is reflected in this document?

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A. The primary - the basic reason

we had during our evaluation of the methods was,
since we decided to use, to prepare our own standards
in saline as opposed to using standards that were
supplied by the manufacturer, we wanted to have at the
beginning control for the stability of digoxin in
these standard solutions of saline.

Q. Yes.

A. So we decided to use one of
the controls in serum supplied by the manufacturer
in each assay to give us a sort of a general check,
quality control check on the stability of our
standards in saline, and subsequently a second
purpose developed to be used as a sort of general
control sample in each assay that might indicate
any major problem with the assay. So that this was
done in each assay subsequently, and since it was
done in so many assays I put this information to-
gether to answer the question that I was asked to
answer.

Q. This was not a separate study
but this was a compilation of data that you accumulated
over the course of many assays in which these controls
were used?



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6

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A. That is right, sir.

3

Q. As I understand what you did,

4

you pooled together a number of digoxin standard

5

serums with a known concentration of 2 nanograms

6

per millilitre, ran those as controls, and I think

7

you said 86 different assays over the course of

8

seven months, and in the result the mean measurement

9

that you achieved on those known concentrations was

10

1.895 nanograms per millilitre.

Do I understand that correctly?

11

A. That is correct.

12

Q. And you have stated the standard

13

deviation there and calculated the coefficient of

14

variation?

A. That is correct, sir.

15

I should perhaps add to it if I may

16

that while I haven't compiled this document up to

17

now, of course, we are looking at the results in

18

each assay that was conducted.

19

Q. Yes. Now your normal RIA

20

procedure as we know calls for extraction. I note

21

that this document records that the assays were

22

carried out without prior extraction of the sample?

A. That is correct, sir.

23

Q. Can you explain to me, please,

24

25



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2

why that was so, why no extraction in dealing with these samples?

3

4

A. As I recall it I felt there was really no need for extraction for the purpose for which this was designed.

5

6

Q. All right. I accept that.

7

A. This wasn't a case sample.

8

This was ---

9

Q. It wasn't a case sample.

10

You were taking as I understand it, what, Red Cross blood. This was straight serum, was it not?

11

12

A. This was a serum, reconstituted serum supplied by the manufacturer.

13

14

Q. The next document is also an intraassay precision study, this time with respect to heart tissue?

15

16

A. That is correct, sir.

17

Q. The notation is this is from control children on previous digoxin therapy.

18

19

The second column records the number of complete analyses done on each sample, does it not?

20

21

A. That is correct, sir.

22

Q. All right. Now this is not heart tissue from the children whose deaths are here

23

24

25



1
2 under investigation?

3 A. No, sir.

4 Q. I take it these were postmortem
5 samples?

6 A. That is correct, sir. These
7 were autopsied - what I have learned the term fresh
8 autopsied samples from control children on
9 digoxin therapy.

10 Q. And by fresh you mean not fixed,
11 not preserved?

12 A. That is right, sir.

13 Q. You understood these were
14 fresh autopsied samples, collected at autopsy from
15 children who had been receiving digoxin therapy in
16 life?

17 A. That is correct, sir.

18 Q. Can you explain for me the
19 results, please? If you will just explain the first
20 line I think we can then understand the other.

21 A. Yes. The first number one as
22 I recall it was either left or right ventricular of the
23 heart. That was the region of the heart that was
24 studied.

25 Q. Yes.

A. And that was extracted four



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times and assayed by the procedure that we - this was done also as I recall it before - during the period of evaluation of our method, and the results obtained at the end by our procedure, RIA procedure, ranged between 56.9 and 62.9 nanograms per gram on this one, on these tissue samples.

Q. Yes.

A. Giving a mean or average of 59.1 and a coefficient of variation between these four results of 4.8.

Q. Now it may not go to the importance of the intraassay precision studies that you were concerned with at the time, Mr. Cimbura, but it may be of interest to us later. Perhaps we could ask you now.

Sample No. 3 apparently when analysed three times produced a range of level from 343.3 to 414.4 nanograms per gram, very much higher levels than those which had been recorded on any assay of Samples 1 and 2?

A. Yes.

Q. Now this too was a child who had been on normal digoxin therapy as you understood it?

A. That is right.

Q. Was this study of any help to you in indicating the range of concentration of



1
2 digoxin that you might expect to find in the heart
3 tissue of children who had been on therapeutic
4 administrations of the drug?

5 A. Yes, sir. Of course this
6 was another purpose of this type of study is to
7 provide me and provide everybody with information
8 as to what is the extent of our values that one could
9 find in infants or children on digoxin therapy, and
10 there was very little information available anywhere
else at that time.

11 Q. It appears from this document
12 at least that the range that you discovered on the
13 average numbers here was from 48.9 to 383 nanograms
per gram?

14 A. That's ---

15 Q. A range of concentrations
16 that you would find in children who had had normal
17 therapeutic administration?

18 A. Yes. After studying, of
19 course, much more children ---

20 Q. Of course.

21 A. - than these two children here,
22 that is the range as I know it now.

23 THE COMMISSIONER: Were all of these
24 taken from the same part of the heart or is there
25



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some distinction?

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THE WITNESS: They were quite often,
sir, taken from the left ventricular although the
right ventricular was also studied sometimes.

5

6

7

THE COMMISSIONER: I just don't under-
stand these numbers, at the left hand column, 1, 2,
3. What do they mean?

8

9

THE WITNESS: I didn't want to refer
specifically to autopsy numbers. 1 and 2 ---

10

11

12

THE COMMISSIONER: It is just one ---

THE WITNESS: 1 and 2 are different
parts from the same child, from the heart of the same
child.

13

14

THE COMMISSIONER: I see.

15

THE WITNESS: And No. 3 is a separate
child.

16

17

THE COMMISSIONER: A separate child.
Yes. All right.

18

19

MR. LAMEK: Q. Mr. Cimbura, did you
have any information about the age of these children?

20

A. Yes, I had information in some
instances.

21

22

Q. Did you know how long they
had been on digoxin therapy?

23

24

25

A. With some of them - this is the



1
12 2 information I was asked, the people who co-operated
3 with me to provide to me, and in some instances I
4 received that information. In other instances I
5 called the people for information and in other
6 instances I went to the Hospital and went through
7 the medical charts and obtained information, so I
have in many cases I have that information.

8 Q. That is right. These were
9 samples I take it you were obtaining from the
10 Pathology Department of the Hospital for Sick Children?

11 A. That is correct, sir.

12 Q. And then we have one other
13 intraassay precision study. This time with respect
to spiked Klotz solution.

14 Now intraassay precision studies I
15 think I am beginning to understand, but why were
16 you interested in doing one on spiked Klotz solution?

17 A. Well, Klotz solution was the
18 solution that was surrounding the specimens that
19 we received for examination from many children, and
20 as a result of that examination the Klotz solution
21 had to be examined as far as what is the concentration
of digoxin in it.

22 Q. And therefore you wanted to
23 know that you could reliably and repeatedly assay the
24
25



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Klotz solution itself for digoxin concentration?

A. That is right, sir.

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Q. And that is the result of that study setting out also the coefficient of variation percentages.

A. That is correct, sir.

Q. Now, in the next document, Mr. Cimbura, it is headed: "Analysis of Postmortem Blood and Heart Disease from Control Children Not on Digoxin Therapy".

A. Yes.

Q. And this arose I think, or the production of this summary arose because as I recall it you were asked, you said that you had also assayed samples from children who had not been on digoxin and had not obtained the same results as those that were being reported by Dr. Seccombe and his team in Vancouver; do you recall that. You said you were not getting positive results?

A. Oh, yes.

Q. When you assayed samples from children who had not been on digoxin.

A. That is correct.

Q. You referred to a study that you had done and you were asked to give us more information about it and this document I take it is in response to that request?



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A. This is in response to the request of course.

Q. Yes.

A. In addition of course this is the type of work that is very important to do as part of the evaluation of the methodology before we start to apply it to the samples, I wanted to make sure that in our results we were getting positive results.

Q. In other words, you not only wanted to be sure that you can measure what is there, we don't want to be measuring what is not there.

A. That is correct.

Q. And as I understand it then, you took samples from some 24 children, blood samples from 24 children; was it from 20 of those you also obtained fresh heart tissue?

A. That is right, sir.

Q. And from four of them you got fixed heart tissue in Klotz solution?

A. Well, from four of them we analyzed fixed, four fixed heart tissues, that's right.

Q. And in two cases there was - Klotz solution had been used in the fixing of the heart tissue.



E3

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A. That was the Klotz solution surrounding the tissue, that's right.

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Q. In terms of blood and fresh heart tissue you have populations of 24 and 20 in terms of sample.

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A. Yes.

Q. And you stated the age range of those children with a breakdown in the right hand column as to the more particular information as to age; in the case of the blood samples 12 were two months old or less; five of those children were premature. Notwithstanding that on your analysis those 24 samples I take it were negative, that is to say you did not record any digoxin, or digoxin-like substance?

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A. Well they were negative below the limit of our usual limit of detection.

20

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Q. Was that 1 nanogram?

A. This is 1 nanogram, usually 1 nanogram per millilitre, that is right.

Q. So negative according to your procedure, the limit of ~~which~~ ^{of yours} detection was 1. In no case was there a reading of anything recorded of greater than 1 nanogram.

A. In blood, that is right.



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Q. Or in anything else?

A. In tissue the detection limit is somewhat higher and to some degree it depends on how much tissue is available for the analysis, but usually I would say on the average our detection limit in tissue would be around $2\frac{1}{2}$, ^{2.7}.5 nanograms per gram.

Q. Now, Mr. Cimbura, what can we infer from those results? Can we infer either that the children from whom these samples were drawn did not happen to have substance X, or anything that cross-reacted with the antibody; or that if it was present it was present in concentrations of less than 1 nanogram a millilitre; or if it was present it did not cross-react with your antibody. Are those inferences that could be drawn from these results?

A. Or was removed by our extraction process.

Q. Or was removed by your extraction process?

A. Yes.

Q. Are there any other inferences of conclusions that can be drawn from this study that you can now think of?

A. Not that I can think of now, no.



E5 1
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3 Q. You were also asked during the
4 course of your first time here, Mr. Cimbura, about
5 the examinations you had made and the studies you had
6 done to determine the cross-reactivity of the Beckman
7 antibody that you were using in your RIA. The next
8 two documents summarize, as I understand it, the
9 cross-reactivity studies that you did with the RIA
10 kit that you were using, is that fair?

11 A. That is correct, the ones we
12 did ourselves, that's right.

13 Q. Can we look first at the cross-
14 reactivity studies on the digoxin metabolites and
15 other of the related substances, can I call them
16 related substances?

17 A. Yes, in a sense that ^{they are} digoxin
18 metabolites and digitoxin metabolites.

19 Q. If I understand this table
20 correctly, digoxigenin-mono-digitoxoside react more
21 than twice as vigorously with the Beckman antibody
22 than digoxin itself; is that right?

23 A. That is correct, sir, 2.3 times
24 more.

25 Q. And the two sugar version of
that molecule reacts 40 per cent more strongly
with the antibody than digoxin itself?



E6

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A. That is correct, sir.

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Q. So although we have an antibody

4

for digoxin in fact those two substances react more

5

strongly with the antibody than digoxin does?

6

A. That is correct, sir.

7

Q. When we get down to the

8

digitoxigenin and the dihydrodigoxin compounds those

react at a very much lower level do they not?

9

A. That is correct, sir.

10

Q. Were these substances which

11

you attempted to screen out by the use of HPLC?

12

A. These and others, that is right.

13

Q. Yes, but certainly these?

14

A. Yes, as I recall it we have

another document.

15

Q. Yes.

16

A. As I recall it these and others.

17

Q. I am not suggesting these are

18

the only ones that you tried to screen out, but each

19

of these ~~other~~ than digoxin itself obviously ~~you~~

20

tried to screen out by HPLC?

21

A. That is right.

22

Q. Did that also apply to

23

dihydrodigoxin, the very bottom one with the cross-

reactivity per cent of .007?

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A. That's right.

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Q. And you attempted to eliminate

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that by HPLC as well?

5

A. That's right.

6

Q. Now, the next document lists

7

a whole series of drugs and other substances, and

8

did you also examine the cross-reactivity of these
substances?

9

A. Yes, sir, these were done in

10

a different fashion. We prepared concentrations of

11

these substances that are mentioned on this document.

12

The concentrations were targeted to be prepared in

13

a sufficiently high range, and as one might encounter

14

let's say in fatal situations.

15

Q. Yes.

16

A. And all the results of these

17

are that when these drug solutions were put through

18

the Beckman RIA assay the results were negative.

19

Q. So on the assay to determine

20

cross-reactivity you found no cross-reactivity of
any of these substances?

21

A. That is right, the results

22

were negative.

23

Q. Did you attempt nonetheless

24

to screen out any of these substances by HPLC? I

25



1
2 must say I can't think why you would if there were
3 not known to be cross-reactive.

4 A. I think somebody may have for
5 other reasons but not for this reason.

6 Q. At least you determined the
7 absence of cross-reactivity with respect to each of
8 the substances on this sheet?

9 A. That's right. The reason
10 fluoride-citrate preservative, maybe the reason is
11 not apparent but this was the blood as I recall it
12 from child Cook was received in a container which
13 contains this preservative, and that is the preserva-
14 tive which we recommend to the pathologist they
15 should put blood into. So the first thought we had
16 we wanted to make sure that does not interfere with
17 the RIA.

18 Q. Mr. Cimbura, we are getting
19 through the fulfillment of the undertakings if I can
20 put it that way.

21 The next document is a graph, and this
22 went to the evidence you gave about fixed tissues.
23 It appears that at some point in your labourious
24 work an attempt was made to determine the stability
25 of digoxin in Klotz solution. Let me be clear we
are not talking about digoxin in a tissue in Klotz



1
2
3 solution, are we, we are talking about the Klotz
4 solution itself if there is digoxin in that, as I
5 understand there may be, it comes out of tissue,
6 it may transfuse from the tissue into the solution,
7 and once it is in the solution you wanted to know if
8 it remained in the solution I take it?

9 A. I wanted to know if it
10 remains in the solution and of course from these
11 results infer a possibility of what may happen in
12 the tissues as well.

13 Q. It may tell you something about
14 that as well. You therefore established a concentra-
15 tion, it looks like 550 nanograms per milligram in
16 the Klotz solution?

17 A. Initially, that's right.

18 Q. And then conducted assays
19 I take it at each of the points along the bottom
20 scale at which points appear on the graph, is that
21 right?

22 A. That's right.

23 Q. The circles and the triangles.

24 A. The same solution actually
25 was studied either at refrigeration.

Q. Yes.

A. Or at room temperature and



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the two graphs reflect that condition.

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Q. And it appears that in each of those conditions the concentration of digoxin over a period of, what is that, nine months, no, a bit less than that seven months, 220 days is it?

7

8

9

A. 221 days, right.

10

11

12

13

Q. What is that about, seven months?

A. Roughly.

14

15

16

17

Q. Decline from a level of 550 to what, about 370 in the case of the refrigerated sample, and to about 150 in the case of the room temperature sample?

18

19

20

21

A. Approximately, yes, as analyzed by the RIA.

Q. By straight RIA, there was no HPLC in this material?

22

23

24

25

A. That's right, there was no extraction.

Q. And if therefore there had been a simple metabolizing of the digoxin in the Klotz solution it would presumably have been measured to some extent in the RIA, would it not?

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28

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A. It is actually metabolites, Mr. Lamek, referred to changes in the body, not



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outside the body.

Q. But there was degradation apparently of this digoxin to the extent where it was not recorded at all, not to the extent of ~~the~~ loss anyway?

A. Yes, as a result of my research that is the conclusion I have reached, especially when Klotz solution usually containing digoxin are stored at room temperature, there is what I believe a chemical degradation of the drug which can produce markedly reduce concentrations after some time, that's right.

Q. Does this study tell you this, Mr. Cimbura; that if tissue is stored in Klotz solution and digoxin in that tissue moves from the tissue into the solution you can't find the original concentration by assaying the tissue, assaying the solution and adding the two together, because it is not going to remain in the solution according to this document, is it?

A. That's right.

Q. So it may be lost?

A. It may be lost due to the vagaries of degradation.

Q. It is not just as simple as



1
2 saying okay, let's measure everything in the bag and
3 we will get what we started with?

4 A. That's correct.

5 THE COMMISSIONER: Doesn't it seem
6 a little extraordinary that at 50 days it seems to
7 recover itself?

8 MR. LAMEK: Yes, it goes up again.

9 THE COMMISSIONER: It seems to go
10 up again, isn't that odd?

11 THE WITNESS: That is right. I have
12 observed that and we have run detail over the
13 analytical - each of these analytical determinations
14 was done very carefully, was done three or four
15 times and I could see no error in the procedure.
16 Certainly it is not what I would normally expect.
17 So the only possible explanation I could offer for
18 that and it is only a theory is that whatever
19 degradation products are produced they may change in
20 this period of time, they may have different cross-
21 reactivity with the digoxin antibody and it is
22 curious that both the room temperature and refriger-
23 ated at the same time there seems to be some re-
24 equilibrium you know of these products.

25 Q. They have a bit of a flurry
and then go into a decline?



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A. That's right.

3

Q. Just one thing I want to be

4

clear about, Mr. Cimbura. You have wiggley lines

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cutting across each of those curves, can you tell

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me what that indicates, please?

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BmB.jc
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A. I intended to indicate with this that the scale on the button is not proportional from that point on.

Q. That is what I had understood. It doesn't mean that your last measurement was taken at 155 days and the rest is mere extrapolation, does it?

A. No, the last measurement was taken at 221 days.

Q. Thank you. And then you did the same exercise, as I understand it, the next document, with embalming fluid. You wanted to find the stability of digoxin there and that I take it is because at a certain point in time you began to receive samples from exhumed bodies, most of which had been embalmed?

A. That is correct, sir. I don't know whether most, some of them.

Q. Some of them had been embalmed. Do I take it here you spiked with a known concentration the sample of embalming fluid?

A. That's right. I had asked the police investigators to provide me with controls from the funeral homes where these children were embalmed and one of these fluids we spiked with digoxin



F.2

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concentration and left the solution or mixture sitting
at room temperature for a period of - indicated on
the document.

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Q. A little over six months, yes.

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A. And re-analyzed them each time

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by RIA.

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Q. Yes.

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A. And again at 197 days and just

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about all the digoxin is lost by RIA.

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Q. Are you able to draw any

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inference, Mr. Cimbura, from this study and from the

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chart that we have just looked at about the effect of

18

either fixing or embalming tissues and the effects

19

that that would have upon the digoxin concentrations

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in those tissues?

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A. Yes, I believe I can draw a

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conclusion and it is possible that degradation,

23

decline of digoxin concentrations also happens in

24

tissues which are soaked with these two solutions.

25

Q. All right. We will explore this

26

later but I take it that has some effect upon the

27

ability to draw any firm conclusions on numbers based

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upon concentrations in fixed or embalmed tissues?

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A. That is correct, sir.

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Q. Yes. Indeed, the next table tells

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us something about that, does it not? It is a comparative analysis of fresh and Klotz fixed heart and lung tissues from controlled children on digoxin therapy. I take it the last question I asked you is precisely what you wanted to find out with this study. Can I understand what is happening here. Let us take Case No. 1 in the left-hand column and read across. You record a fresh specimen of heart tissue. LV I take it means left ventricle?

A. That is correct.

Q. Now, let us forget about the result for a moment. You've got a fresh specimen of the left ventricle of that patient's heart, and by fresh you mean unfixed? It is not put in any preservative or fixative?

A. That is correct, and which I received fairly soon after the autopsy.

Q. All right. Now, when I move across to the right-hand side of the table under the heading "Klotz fixed specimens" is the first item under that a further sample of the left ventricle of the same heart but which has been placed in Klotz solution?

A. That's correct, placed in Klotz solution for a period of time, that's right, yes.



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Q All right. And the period of time is stated at the bottom in Note 5 to be six to nine months?

A Depending on these seven cases, that's right.

Q And so as I read each one of these across the fixed and the fresh tissues are from the same heart? Do I have that correctly?

A That is correct, sir.

Q And do I therefore understand, looking at Item 1, that a concentration in the fresh heart of that child, left ventricle of 383 is reflected by a concentration of 6.7 after another sample of that same portion of that same heart had been in Klotz solution between six and nine months?

A That is correct, sir.

Q And similarly, Item 2, a concentration of 250 in the fresh sample becomes 3.7 in the fixed sample?

A That is correct, sir.

Q Indeed, when I look at Item 5 much lower concentrations in the fresh sample of 49 and 59 in the left and right ventricles respectively, after six to nine months in the Klotz solution show negative results?



F.5

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A. That is correct, sir.

3

Q. No measureable digoxin in the

4

fixed tissue?

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THE COMMISSIONER: I am sorry, where
did you get the 383? Was that implanted?

6

7

THE WITNESS: No, that was a child who
was on digoxin therapy, sir.

8

9

THE COMMISSIONER: That specimen, was
that tested after?

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11

THE WITNESS: And then following the
autopsy I have received ---

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THE COMMISSIONER: That was right at
the time of the autopsy?

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THE WITNESS: Well, closely after the
autopsy.

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THE COMMISSIONER: Yes, I see.

17

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THE WITNESS: I received that sample
in my laboratory and we analyzed it at that time and
gave a reading of 383.

19

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THE COMMISSIONER: And after storing
it in the Klotz solution?

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22

THE WITNESS: After the remainder of
the heart was stored in a Klotz solution.

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THE COMMISSIONER: Yes, six to nine
months, registered at 6.7?



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THE WITNESS: That is correct, sir.

MR. LAMEK: Q Now, can we go back for a moment to something we were talking about in relation to the stability of digoxin in the Klotz solution. The extreme right-hand column, Mr. Cimbura, records the results I take it of the assay of the Klotz solution in the case of each of these samples?

A. After the period of storage.

Q. After the period of storage. I suggest it is clear even to me that a level of, and I am looking at Sample No. 1, of 3.1 nanograms per millilitre in the Klotz solution doesn't account for the drop in concentration from the fresh to the fixed heart tissue itself?

A. Well, I haven't provided the data for this purpose. To be able to answer that I would have to look at the volume of the Klotz solution in each of these children.

Q. On the basis of your graph you wouldn't expect to account for the loss, would you?

A. No, I wouldn't expect it. I have that information somewhere but I wouldn't expect it, that's right.

Q. But in any event, although there is no numerical or arithmetic relationship that I



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have been able to work out between the fresh and the fixed heart results, there is in every case a dramatic decrease in the digoxin measurement as between fresh and fixed specimens from the same region of the same heart, is there not?

7

A. That is correct, sir.

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Q. Now, unhappily, we can't say the same with certainty with respect to lung specimens because the two fresh specimens apparently were not assayed in fixed condition and those that were fixed were not assayed when fresh?

12

13

A. That is correct. They were not available due to some reason or another.

14

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Q. That's right. And was this study performed - well, I had better ask you - at what stage of your work was this study performed, Mr. Cimbura?

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A. Well, I don't have the exact time frame here, but as I recall it -- I don't have the time frame, Mr. Lamek, I would have to look it up. It could have been very early, post this proceeding for quite a while, but I don't have the time frame.

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Q. Now, the next sheet is in a sense a continuation of that, is it not, respected in this case the regions of the heart "Regions of Heart",



F.8

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recording Results of Analysis in fresh and fixed samples, again I take it from the same region of the same heart?

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A. That is correct. The essential difference between the two, the previous one and this one was that in the previous one mainly intact organs or heart were placed into the Klotz solution.

8

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Q. I see.

A. And the second experiment only isolated regions of the heart were placed into the Klotz solution. That is essentially the difference, that is right.

13

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Q. Well, there is another important difference too is there not, Mr. Cimbura? In this case the period of storage in the Klotz solution was only one to two months?

17

18

A. That is correct, sir.

19

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22

Q. As opposed to six to nine months in the previous study?

A. That is correct.

23

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Q. But even after one to two months there is an obvious and a clear dramatic drop in the recorded levels of digoxin in the various samples, is there not?

A. That is correct, sir. There is always a drop.



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Q. Perhaps the most dramatic is Sample No. 11 wherein the fresh heart right ventricle the level of 381 was recorded after a month or two's fixation in Klotz solution, 10.3 was recorded in the sample from the same area of the same heart?

A. That is correct.

Q. Again, Mr. Cimbura, did you have information as to the age of these children, the period of time they had been on digoxin, anything of that sort?

A. Yes, with some of them, yes.

Q. I take it it was not important for the purpose of measurement?

A. Not for this particular purpose of this experiment, that's right, other than I wanted these children to be generally children to compare them to the case material.

Q. Yes. Then we come to a comparison of the RIA and HPLC results. This arose out of your evidence as to the purpose of HPLC and the hoped for consequences of running HPLC before RIA.

First, this was done in methanolic solution. What is methanolic solution and why was it done in that, please?

A. Methanolic solution refers to



F.10

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spiked digoxin and methyl alcohol.

3

Q. What is the significance of

4

using methyl alcohol as the medium?

5

A. Well, one significance would be

6

that this was the medium that we used for injection
into the HPLC instrument.

7

Q. All right.

8

A. Another significance would be

9

that our HPLC standards were made up in methanolic
solution.

10

11

Q. I see. Now, the curious thing

12

about this is that in each of the three cases the RIA
after HPLC produced a higher level than it did before
the HPLC. I would have thought your expectation was
to the contrary?

14

15

A. Oh, yes. In principle you

16

cannot get a higher result after HPLC. So that I

17

attribute these two to variations, analytical

18

variations. Another consideration of course is that
whenever we use HPLC for case material it is never

19

on an unextracted sample such as this was, we always

20

use extraction before the HPLC. But the variation

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is, I think it is an analytical variation and in a

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sense when I designed this experiment the purpose of

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it was to tell me essentially whether at its simplest

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form, this is the simplest form of the procedure, whether the two methods are consistent with each other and they certainly are from this to me.

Q All right. Well, those results are not what anyone would have expected I suppose but I hear you and you have produced them and thank you.

The next document however shows a comparison where the medium is blood. Here, it appears at least that the HPLC has performed as you expected it to and has apparently removed some elements with the result that the subsequent RIA produces a lower level than the original RIA. Is that what appears to be happening?

A Well, again, sir, since digoxin was analyzed, pure digoxin was analyzed, ideally those should be exactly the same. I think the fact that the results before HPLC and after HPLC are somewhat different is just an analytical variation.

Q That doesn't indicate that HPLC has screened out some cross-reactive material?

A I don't believe so necessarily.

Q Or it doesn't necessarily mean that?

A It doesn't necessarily mean that.
We started with pure digoxin and blood.



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2 Q. Did you run any compara-
3 tive -- well, yes, of course you did. We will come
4 to those when we get to the actual results, compara-
5 tive studies on actual samples of natural, not
6 spiked, blood. Of course you did. We will come to
7 those showing the difference between pre and post HPLC
8 results.

9 Okay, now, Mr. Cimbura, those I
10 think are the matters that you undertook to dig into
11 and to provide for us. I know that you have done
12 other research studies about digoxin levels. They
13 make up the balance of Exhibit 213. I want to come
14 back to those towards the end of your evidence, and I
15 would like to turn now to the analysis of samples
16 from children whose deaths are here under review.

17 And since I am about to do that,
18 Mr. Commissioner, is this a proper time to take a
19 break?

20 THE COMMISSIONER: Yes. We will
21 take twenty minutes now.

22 --- recess.

23 --- on resuming.

24 MR. LAMEK: Q. Mr. Cimbura,
25 we were about to turn to your analyses of the samples
that you received from the various children whose
deaths are under review in this Commission.



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You told us last time that when the police first brought specimens to you for digoxin assay which was in the week of March 23, 1981, you were initially reluctant to undertake the task because, as I understood you, the Centre had had no experience with the use of the RIA for digoxin assay, especially in spades, with respect to tissue analysis. Did I understand that?

A. Yes. As I recall it the reluctance was mainly with respect to those tissues that were received preserved in Klotz solution.

Q. Yes, because as we will see those were the very first samples that you received, were they not? Well, we will come to that in a moment. That is your recollection, is it not?

A. That is my recollection, that is right.

Q. And indeed you sent the police away and you returned the samples to them the day after they were delivered to you, as I understand it, but they came back later in that week because they couldn't find anyone else who could undertake this task and you agreed that you would do it at the Centre.

Have I summarized that reasonably



1
2 accurately?
3 A. Yes, we agreed we will
4 attempt to do it with the provision that we are
5 given some time to do --
6 Q. Yes.
7 A. -- some developmental,
8 some research, yes.
9 Q. Now I understand, Mr.
10 Cimbura, that when a specimen is brought to the
11 Centre for Forensic Sciences for examination in the
12 Toxicology Department, and is accepted for analysis,
13 it is identified and given a number and a submission
14 slip or submission form is completed. Is that so?
15 A. The submission form is
16 usually completed at our central receiving office.
17 Q. Yes.
18 A. Which is separate physi-
19 cally from the Toxicology Laboratory.
20 Q. I am going to show you,
21 Mr. Cimbura, a bundle of some 22 submission forms
22 in respect of specimens from certain of the children
23 with whom we are concerned. They are all dated in
24 the period between March 23, 1981 and November 1,
25 1982.

I take it you recognize that



G4 2 bundle of submission forms?

3 A. They all appear to be
4 the submission forms from our investigation with a
5 case number, a lab case number, 1549/81.

6 Q. Yes. Do you have a
7 copy of those with you?

8 A. Yes, I believe I have.

9 Q. Why don't you keep that
10 one in that order and I will mark this, Mr.
11 Commissioner, if I may, as the next exhibit.

12 THE COMMISSIONER: 214.

13 --- EXHIBIT NO. 214: 22 Submission Slips.

14 MR. LAMEK: Q. Now unhappily,
15 Mr. Cimbura, in the copying the manuscript portion
16 of some of these slips came out more clearly than
17 the printed portions. I would like just to under-
18 stand the information that is set out on the form.

19 About one-third of the way down
20 the right-hand side in a box the printing of which
21 isn't clear on the first form, but on the second
22 in the bundle it is not bad. There is an indication
23 of the date of receipt of the sample referred to on
24 this form, is there not?

25 A. That is correct, sir.

"Date received", yes.



1
G5 2 Q. And indeed looking back
3 to the comparable place on the top form in the
4 bundle the time is stated as well: 23/3/81. 2:10
5 p.m.
6 A. That is right.
7 Q. And then there is a
8 notation T-12-15-3:15 p.m. Do you see that on the
9 first form in the list, in the bundle?
10 A. That is right.
11 Q. In the box on the left-
12 hand side there are, as I understand it, first
13 the name of the person or persons submitting the
14 sample. In this case Staff Sgt. Sangster and
15 Sgt. Barbour. I'm looking at the first one in the
16 bundle.
17 A. Yes, that is correct.
18 Q. And below that the names
19 of the persons involved in the investigation,
20 Staff Sgt. Press and Sgt. Warr.
21 A. That is correct.
22 Q. The right-hand side there
23 is a place for Crown Attorney which on this
24 document is not completed, and below that, Coroner,
25 Dr. Paul Teperman.
A. That is correct.



G6

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Q. Do you see that?

3

A. Yes.

4

Q. As I understand it,

5

looking at the first document in the bundle, Mr.

6

Cimbura, the request that was made of the Centre

7

with this submission form is really stated in two

8

places: first, just about half way down the form

9

in manuscript, "Investigating unusual deaths - we

are interested in level of digoxin".

10

And then at the very bottom of

11

the form, "Analyze each tissue and each fluid for

12

digoxin".

13

That is what you are being asked

14

to do with respect to the samples listed on this

form, is it not?

15

A. That is right.

16

Q. And the list of samples,

17

according to the form at least, begins in the lower

18

third of the page; the printed heading is "List Items

Submitted".

19

A. That is correct.

20

Q. And they are items

21

numbered 1 through 11. The child's name is set out,

22

then there is an CFS number. Can you tell me what

23

that number is, please.

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A. Yes. This is a seal, a strip of paper with a number used as a seal for containers or items. Sometimes -- quite usually the investigating officers would use the seal or on other occasions the seal may be placed on an item at the receiving office of the Centre, and the purpose of the seal is to -- is a chain of continuity of evidence, and also identification of an item.

Q. All right. So each of those eleven items is given the SFS number and then each is identified: heart, heart, heart and lungs and so on.

A. They are described, that is right.

Q. And then it appears from a portion of the form that we first looked at that T-12-15, four additional samples were received later that day, and are those the ones that are listed in the middle of the page, 12, 13, 14, 15?

A. That is right.

Q. CFS numbers, and were apparently part bottles of digoxin and digoxin tablets or pills?

A. That is right.



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Q. That is what they were?

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A. That is correct.

4

Q. Will you just turn over

the page to the next submission form.

5

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That is also dated 23/03/81. The items submitted are listed in the bottom third of the page as being heart blood samples, one with an anticoagulant and without an anticoagulant, a heart muscle sample and a lung sample, and they are all, as I understand this form, referable to Justin Cook whose name appears in the top right-hand corner.

12

A. That is correct, sir.

13

14

Q. These were delivered to

the Centre by Dr. Cutz.

15

A. That is correct.

16

Q. That is the Dr. Cutz

17

who is the pathologist at The Hospital for Sick Children?

18

A. That is right.

19

Q. And on that form in the

20

lower third of the page, "Examination requested" says, "Drug screen including digoxin".

21

22

A. That is correct.

23

Q. And that is I take it what

24

25



1
G9 2 Dr. Cutz wanted the Centre to do with the samples
3 he had submitted?

4 A. That is correct.

5 THE COMMISSIONER: I can't find
6 that, but I should find it.

7 MR. LAMEK: The lower third of the
8 page on the right-hand side, Mr. Commissioner.

9 THE COMMISSIONER: Oh, yes.

10 MR. LAMEK: The printing is
11 "Examination requested".

12 THE COMMISSIONER: Yes.

13 MR. LAMEK: Q. Now that is
14 23/03/81.

15 On the right-hand side of the
16 middle of the page, Mr. Cimbura, there is some
17 manuscript under the date, 17/9/81 (September 17) -
18 is that your handwriting, are those your initials,
19 GC?

20 A. Yes.

21 Q. And it reads, "Drugs
22 involved", with a list of drugs. Can you tell me
23 what that list indicates?

24 A. That as I am trying to
25 recall -- I am not sure whether I initiated, whether
I have initiated a phone call to Sgt. Warr or he



1
G10 2 phoned me, but it is information that I obtained
3 from Sgt. Warr as I recollect it about drugs which
4 were involved in the treatment of Baby Cook.

5 Q. So that you would know
6 which drugs to look for in your drug screen I take it?

7 A. Yes. This would
8 facilitate our drug screen because drug screen is
9 not a magical word.

10 Q. Yes.

11 A. Certain drugs do not
12 lend themselves to drug screen.

13 Q. Now we have just looked
14 at these two forms. For the sake of understanding
15 the structure of the thing, Mr. Cimbura, on each
16 of them tissue samples were submitted for analysis,
17 but on neither of them do I see any indication of
18 whether the tissues were fixed or fresh, as you
19 have defined that term.

20 I take it it was important to know
21 the condition of the tissue that you received?

22 A. Yes.

23 Q. Was that recorded in
24 some other place?

25 A. Yes. I have probably
26 described it somewhere else in my notes because I have



G11 1
2 observed tissue, that is part of my usual practice
3 in a potential homicide investigation but I am
4 responsible for to look at the specimens I receive
5 and so I have observed them and I have tried to find out
6 what type of tissues they are and what are the
7 fluids involved and so on.

8 Q. All right. When we
9 look at the second form in this bundle in which
10 as we have said one of the items submitted was a
11 sample of heart muscle and another was lung sample
12 and there is a notation "small pieces".

13 I take it you accepted that
14 description of identification of the samples that
15 were submitted, Mr. Cimbura, unless it was obviously
16 wrong?

17 A. That is right. I am not
18 a pathologist.

19 Q. No.

20 A. And I have a piece of
21 tissue; I rely on the description given by the
22 pathologist who brought the tissue.

23 Q. No doubt if they sent
24 you something and said it was liver but it looked
25 like a finger nail to you you might raise some
question?

A. Oh, yes.



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Q. But otherwise you accept the description as it is given to you by the person submitting the sample?

A. That is right. And as a matter of fact I have followed this up with a telephone conversation with Dr. Cutz in any case.

Q. All right. With respect to the hearts and hearts and lungs which were apparently delivered by Sgts. Sangster and Barbour on the first form in the bundle, were those more or less complete organs that were delivered?

A. More or less in a general term. Again I haven't done complete microscopic study on them to find out you know --

Q. Yes.

A. -- to find out what was missing. But some of them, at least some of them looked to me to be fairly complete.

Q. The eleventh item, for example, purports to be heart and lungs, Justin Cook. We know from having looked at the second submission form that a further sample was submitted there which was a small piece of heart muscle from Justin Cook?

A. Yes.



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GL3 2 Q. Which suggests I take
it that the heart and lungs submitted on the first
submission form wasn't entirely complete: there was
at least one sample that was submitted later that
day by Dr. Cutz himself?

A. Oh, yes.

Q. Yes.

A. And the way I understand,
and having discussed that with Dr. Cutz, the
tissue on the second submission form was a tissue
he took before the remainder or fairly complete
remainder of the heart was placed in the Klotz
solution.

Q. Were the organs that were re-
ceived on the first submission form all fixed in Klotz
or some other preservative solution?

A. Yes. They are further
described in my report as I recall it.

Q. Yes.

A. They were all, yes, that
is right.

Q. What about the small
tissue samples that were delivered by Dr. Cutz
himself under the second submission slip, were they
fresh or fixed samples?



G14 2

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A. They were what I call
now as fresh, that is right.

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Q. Of course we know if we
go through all these forms that you received not
merely blood and tissue samples. Indeed the very
first form records that part bottles of digoxin were
submitted to you for analysis.

8

A. That is correct, sir.

9

10

Q. You analyzed those for
digoxin content?

11

A. That is right.

12

13

14

Q. When tissues were
delivered in preservative or fixative did you
analyze the preservative or fixative for digoxin
content?

15

16

17

A. Yes. As a rule as I
recall it. Again it is in my report but, yes, we
have.

18

19

20

21

Q. All right. Now could
you flip through this bundle please, Mr. Cimbura,
and there are three submission slips, each dated
June 25, 1982. 25/6/82. They are towards the
end of it, and there are three one after the other --

22

A. I have it.

23

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Q. The first one is in



ANGUS, STONEHOUSE & CO. LTD.
TORONTO, ONTARIO

Cimbura
dr.ex. (Lamek)

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respect to Barbara Gionas. That is the name in
the top right-hand corner.

A. That is correct.



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Q. The next one Kristin Inwood;
and the third one of that date, Brian Gage, do
you have those?

A. That is correct.

Q. Now those appear to be
samples of embalming fluid, do they not?

A. Yes. The first form is three
samples of various fluids reported to have been used
in embalming of ---

Q. Of Barbara Jones?

A. Of Barbara Jones, that's
right. The second one also with respect to Kristin
Inwood?

Q. And the third one embalming
fluid?

A. That's correct.

Q. Embalming fluid used in respect
of Brian Gage?

A. That is correct.

Q. This I take it is about the
time that you are receiving tissue from children
whose bodies had been exhumed?

A. About, I cannot recall if
it was before or after, that's right.

Q. The form, the submission form



Cimbura, dr.ex.
(Lamek)

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records that you requested that the investigators obtain a sample of the embalming fluid for a controlled sample, and you made that request?

A. That's correct.

Q. And these samples were collected from several funeral homes by the police officers and delivered to you?

A. That is correct.

Q. And did you indeed analyse the embalming fluid?

A. Yes, as stated in my report, I can't recognize all of them, but as I recall it we have, yes.

Q. So we had a wide range of samples of materials that were analysed in the course of your work on this particular test, Mr. Cimbura?

A. Yes.

Q. Just going back to the very first form, perhaps it becomes clearer from the second and third sheets in the bundle, Mr. Cimbura. Sheet No. 2, four items were submitted; two blood samples, a heart muscle sample and a lung sample. They are numbered in the first place 1, 2, 3, 4 down the left hand side, and then to the left of that I see T-40, 41, 42 and 43, are the T numbers the internal



1
2 identification of the numbering system in the
3 Toxicology Department of the Centre?

4 A. Yes. T refers to Toxicology
5 and the T numbers would be assigned to items examined
6 in Toxicology, that's right.

7 Q. And they are referred to in
8 those numbers, the T numbers when you get to your
9 reporting stage, are they not?

10 A. That is correct.

11 Q. And if we turn over to the
12 next sheet we see T-20 to T-23, this time happily in
13 typed script is the sample submitted?

14 A. That is right.

15 Q. Now, the digits on my review
16 of these submission forms and the reports Mr. Cimbura,
17 go up to 112, there are however no capital T numbers
18 for No. 16, 17, 18, 19, 38, 39 and 94. Can you tell
19 me please why there are those gaps in the sequential
20 numbering of these samples, are we missing some
21 samples?

22 A. Are these the numbers that
23 Mr. Marshall asked me to check?

24 Q. Yes.

25 A. Well okay, in that case I have
checked those numbers and there are numbers which were



1

2

not used.

3

Q. You didn't use them?

4

4

A. They were not used to assign

5

a T number to these specimens, that is right.

6

Q. Is there any particular reason

7

for not using them?

8

A. Well, as I recall I think

9

we were receiving samples with some frequency and

10

I may have had a concern to leave some overlap between

11

the previous to the next so if similar items may come

12

in we may use those numbers, or it may have been just

13

my lack of memory on what the last number assigned

was.

14

Q. You are the way I am with

15

exhibits, what was the last number, never mind let's

16

give it this one.

17

All right. But at least we can be

18

sure that the gaps in the sequential numbering don't

represent lost or mislaid samples?

19

A. That is correct, sir.

20

Q. Now we have also marked as

21

an exhibit in this Inquiry, Mr. Cimbura, your reports

22

setting out the results of your analysis and that is

23

Exhibit 95, Mr. Commissioner, 95A through I believe

24

F. Do you have those reports with you, Mr. Cimbura?

25



1

2

A. Yes.

3

Q. Let me show you-first of all,

4

Mr. Cimbura, I have no intention of going through every one of these results on each and every one of these samples on each and every one of these children. I want to understand the form of your reports, and then perhaps just a few questions about some of the results.

9

10

11

I take it that the analyses, of the results as set out in your reports Exhibit 95 were conducted according to the procedures that you have described for us?

12

13

A. That is correct, sir.

14

15

16

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18

19

Q. Now, the results are not numbered sequentially by sample number in these reports, they tend to be grouped by child within each report if I understand it, and that makes sometimes a little difficulty of concordance with the submission forms and the reports but we can cope with that.

20

21

22

23

24

25

I am interested in the formulation of your results and your reports, Mr. Cimbura. In the first report which is dated January 11th, 1982, could you turn with me please to page 11. Now, at the top of page 11 you are referring to Sample T-4



1
2 which, turning back a page, was alleged to be the
3 heart of Michael Fanjoy. Now Fanjoy is not a child
4 with whom we are concerned and I am not interested
5 in the results so much as the formulation of the
6 report. At the top of page 11 you report on your
analysis of the heart:

7 "The left ventricular the tissue was
8 found to contain 15 nanograms calculated
9 as digoxin/or digoxin like substances."

10 Do you see that formulation of your
11 report. Why do you express your report in that way?
12 Does that tell me anything about the analytical
13 procedures that you used in analysing that tissue?

6
14 A. Yes. This would tell me for
15 this particular analysis we used only the RIA
procedure at that time, it describes it.

16 Q. And having used only the
17 RIA you did not know whether what you were recording
18 was digoxin or digoxin like substances, or a
19 combination of them?

20 A. That is correct, sir.

21 Q. And therefore that form of
report indicates analysis by RIA alone?

22 A. That is correct.

23 Q. Can we turn back to page 9,
24
25



Cimbura, dr.ex.
(Lamek)

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7 please, of the same report. You are reporting on
page 9 on Sample T-9 the heart and lung that was
submitted of Charlon Gardner.

A. That is right.

Q. And then with respect to the
left ventricular you say:

"The tissue was found to contain 117
nanograms per gram calculated as
digoxin of a mixture of digoxin and
digoxin like substance or substances,
the concentration of digoxin was one
one nanograms per gram."

Can you tell me please whether that
form of report indicates the analytical procedures
that were used on that sample?

A. Yes, sir. In this instance
we have used both the RIA procedure and the RIA
after HPLC separation procedure and the results
between the two were different, and from other
information and research I have done I have concluded,
that there is not only digoxin present but there is
also digoxin like substances and I have accordingly
separated the findings into the findings by IRA
and findings by HPLC.

Q. So that form of report indicates



1
2 that there was initially RIA analysis which resulted
3 in that particular case of a level of 170 nanograms
4 per gram; that there was then a separation of the
5 sample by HPLC and upon subsequent RIA the reading
6 was one for one nanograms which you now express as
7 digoxin believing the digoxin like substances to
8 have been separated out by HPLC, do I have that
correct?

8 9 A. That is correct, sir.

10 Q. So that form of report means
11 RIA/HPLC/RIA?

12 A. No, it may mean RIA/RIA/RIA-
HPLC after HPLC.

13 Q. Yes. Now let's go back to
14 page 11 because we have got yet another formulation
15 of the report on page 11. The lower half of the
16 page you are reporting on the analysis of Sample T-35?

17 A. Yes, sir.

18 Q. With respect to the left
19 ventricular of Amber Dawson's heart you report:

20 "The tissue was found to contain 19
21 nanograms per gram estimated as
22 digoxin calculated as digoxin or
23 digoxin like substance or substances
no digoxin could be detected."

24
25



1
2 Can you tell me what that indicates,
3 if anything, about the analytical procedures used?

9
4 A. That indicates that both the
5 RIA and RIA after HPLC are conducted, the HPLC result
6 was negative, therefore indicating there is no
7 digoxin.

8 Q. You mean the RIA after HPLC?

9 A. Yes after HPLC was negative,
10 yes.

11 Q. Yes.

12 A. The RIA before HPLC the result
13 was 19 nanograms per gram.

14 Q. So in that case I may take
15 it once again you did RIA/HPLC/RIA?

16 A. That is right, sir.

17 Q. The second reading produced
18 a negative and you therefore inferred that the HPLC
19 had separated whatever had been reacting with the
20 antibodies on the initial RIA?

21 A. That is what I concluded,
22 that's right.

23 Q. I am interested in all these
24 things, Mr. Cimbura, even when reporting the result
25 of the initial RIA procedure you expressed the
result as being "calculated as digoxin", what do you



1

2

mean by those words?

3

A. The digoxin standard curve

4

was used for the calculation.

5

Q. That's all?

6

A. That's all.

7

Q. That is not a means of

identifying whatever you are finding?

8

A. No.

9

Q. And then finally we have got

10

I think the only other version of a report that I

11

have seen, I'm sorry, I am referring to page 2 of

12

the same report.

13

A. Page 12?

14

Q. Page 2, please; the second page

15

of that report of January the 11th, 1982. Sample

16

T-27 just half way down the page was a sample of

17

yellowish fluid reported to be serum from Justin

Cook, and your report is:

18

"The fluid was found to contain 46

19

nanograms per millilitre of digoxin."

20

Now what does that tell me, if any-

21

thing, about the analytical procedures used?

22

A. That indicates that both RIA

23

and RIA after HPLC studies were done on this

24

specimen and that the results were considered

25

10



1
2 consistent and therefore the conclusion I reached
3 that it is mainly digoxin.

11 4 Q. So the simple statement of a
5 finding of digoxin as a steady concentration indicates
6 RIA/HPLC/RIA but the two RIA results are corroborative
7 of each other, consistent with each other, and
8 therefore you don't report them separately as being
9 digoxin and something else and then just digoxin?

10 A. That is right within analytical
11 limits.

12 Q. But again I must take that
13 as meaning HPLC before the final RIA?

14 A. Pardon me?

15 Q. You did the HPLC before the
16 final RIA?

17 A. Yes.

18 Q. In that form of reporting?

19 A. That is right.

20 Q. And then I think really the
21 last formulation of a report that I find is on page
22 3, the next page over. Sample T-20 is described as
23 a sample of a thick fluid material in a jar bearing
24 certain seal numbers labelled "Small bowel contents
25 Justin Cook" reported to be part of small bowel and
contents.



BmB.jc
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Q. On your report there, it reads a total of 621 nanograms of digoxin was found in the material submitted. It is not a concentration by unit it purports to be a global statement of the aggregate digoxin in the entire sample, does it not?

A. That is correct, sir.

Q. Now, why is that reported in that way?

A. Well, the reason may vary depending on the approach and time and so on but in this particular sample, as I recall it, through the various stages of the examination of the sample I concluded that the sample is not homogeneous, therefore, one cannot express the concentration in the usual way. If the sample is not homogeneous with respect to digoxin, each different portion of the sample may have different concentrations.

Q. Yes.

A. Because of that conclusion, which was based on the results of Warner, I have decided that we should combine individual measurements obtained and combine these as a total that was found in the amount of the sample received, done by us.

Q. You mean in fact you assayed the whole of the sample?



I.2

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A. That's right.

3

Q. And added the results together?

4

A. That's right.

5

Q. And does the fact that the

6

result is stated to be 621 nanograms of digoxin

7

indicate here, as it did in other reports, that the

8

procedure on each portion of the sample included HPLC?

9

A. That's right. Oh, I'm not sure

10

whether on each of the samples; at least one of the
samples.

11

Q. All right.

12

A. One of the portions of the samples.

13

Q. One of the portions of the samples,

14

all right.

15

While we are on page 3, can we go to

16

another aspect of these reports about which I would
like your comment, Mr. Cimbura.

17

At the very bottom of the page, having

18

reported the results of all of the Cook samples which

19

were included in this report, you have a note, and

20

the note continues on to page 4. Now, I want to come

21

to those notes, but before I do, let me ask you this.

22

As a forensic toxicologist, are you required to be

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aware of the threshold of toxicity for the various

24

drugs whose presence you are asked to detect and

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measure?



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A. I'm not exactly sure what you mean by threshold?

Q. Well, do you need to know whatever is believed to be the range of toxic concentrations?

A. That's right, oh, yes, certainly.

Q. And do you regard that information as falling properly within the area of expertise of a forensic toxicologist?

A. Yes, sir.

Q. I am sure you have given evidence in court on a number of occasions, Mr. Cimbura?

A. Yes, I have.

Q. On such occasions are you permitted to state an opinion as to the range of toxic levels of the drug in question?

A. Yes.

Q. On what do you base those opinions?

A. Well, depending on the drug of course, there are thousands of drugs.

Q. Well, let's take digoxin, for example.

A. Well, digoxin, I would base mainly that opinion on the result of my research that I have conducted on infants on normal doses of the



I.4

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drug with respect to the threshold of the normal range.

3

Q. Yes.

4

5

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A. And with respect to the fatal range, this would be based on published literature, results of peer forensic toxicologists in past cases investigated of digoxin poisoning.

7

8

9

10

Q. And when you appear as a witness, as a toxicologist in court, are you permitted to say whether the levels which you have measured fall within what in your opinion are the toxic ranges for the drug?

11

12

A. Well, I cannot specifically recall. I would expect to, yes.

13

14

Q. Yes.

A. I have no reason to - I have no recollection it was not allowed anywhere.

15

16

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Q. And in the case of fatal poisoning, are you permitted to express an opinion as to whether the drug levels that you have measured are consistent with death having been consistent with intoxication by that drug?

20

21

22

A. Oh, yes. Well, most of these investigations of course in our line of work would refer to coroners' inquests and certainly there, oh, yes, yes.

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Q. Now, when you add notes to a



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report such as the one we are now looking at, Mr. Cimbura, is it your purpose to assist the recipient of the report in understanding and interpreting the concentrations that you have reported?

A. That's right. The purpose of a forensic toxicologist is to assist pathologists, investigating officers with toxicological interpretation or the findings.

Q. Could we look at the note that you in fact wrote on these Cook samples. It starts at the foot of page 3:

"(1) Concentrations of digoxin found, research at the Centre, in postmortem specimens of blood of infants and children on digoxin therapy range between 0.5 and 9.7 nanograms per millilitre."

I take it that you had conducted some research at the Centre of Forensic Sciences that enabled you to state that range?

A. That is correct, sir.

Q. Now, I will be coming to that study a little bit later.

A. Yes.

Q. But it is something about which



I.6

1

2

you will tell us today, is it?

3

A. Yes, that the research continued,

4

so, actually the range now is different than it was then.

5

6

Q. But as it then existed that was the range that emerged from your study?

7

A. At that time, that's right.

8

Q. Over on the next page. You

9

report in Note 2:

10

"(2) The concentrations of digoxin

11

in the blood, Sample T40 and T41 and

12

in the serum T27 are within the range

13

of values reported in blood or serum

14

from cases of fatal poisoning (13.8

15

to 200 nanograms per millilitre)."

16

And that I take it is based upon your review of the literature?

17

A. That is correct, sir.

(2)

18

Q. Rather than on any independent research of your own?

19

A. That's right. These are cases

20

of fatal poisoning and these are based on published

21

literature, that's right.

22

Q. And as at the time you were

23

writing this report, that was the range of numbers

24

25



I.7

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which in the literature appeared to have been

3

measured in cases of fatal poisonings with digoxin?

4

A. That is correct, sir.

5

Q. And similarly Note 3, and I won't

6

bother to read it, perhaps you could just cast your

7

eye on it, appears to be based both on your own

8

research and on a literature review?

9

A. That is correct, sir.

10

Q. As does Note No. 4?

11

A. That's right, sir.

12

Q. And therefore you provide not

13

merely the numbers but also such guidelines as you

14

think may be relevant to the reader of the report,

15

either based upon your own research or upon the literature

16

as to what those numbers may mean?

17

A. That is correct, sir.

18

Q. All right. Another thing in the

19

report that I would appreciate an explanation of, Mr.

20

Cimbura. Could we go to page 7 of this first report.

21

On page 7 you are completing the report

22

on a number of samples starting on page 6 from Jordan

23

Hines. T6 had been heart tissue, T44 liver tissue

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from exhumation and T45 muscle from exhumation, and

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you report upon your findings in those samples. Then

you say:



I.8

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"Note: (1) From the data derived from T6 (that's the heart sample) it is estimated that the concentration of digoxin in the heart before it was fixed in the Klotz solution was not less than 252 nanograms per gram."

Now, can we put that in context. Let us turn back to page 6 for the moment, Mr. Cimbura. T6 is the heart of Hines. This you had received initially back on March 23rd, it is one of those referred to on page 1 of the very first submission form, you will remember?

A. Yes.

Q. This was a fixed organ, was it not?

A. Yes.

Q. It was in Klotz solution?

A. That's right.

Q. This wasn't exhumed tissue, this was fixed from autopsy?

A. Yes.

Q. And you were reporting on that and you found in the left ventricle, you say digoxin after HPLC of 52 nanograms per gram, and top of page 7 you found in the right atrium 45 nanograms of digoxin and/or digoxinlike substances, in the septum



I.9

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89 nanograms per gram of digoxin, and then you measured the Klotz fluid surrounding it. And you say, from that sample T6:

"It is estimated that the concentration of digoxin in the heart before it was fixed in the Klotz solution was not less than 252 nanograms per gram."

And I would like to know please how you make that estimate?

A. Yes, the numbers that I needed to make that estimate were the concentration of the Klotz solution, which I have, the volume of the Klotz solution, which was surrounding the organ, which I had, which I measured. From those two values I could calculate a total concentration of digoxin and/or digoxinlike substances and the Klotz solution surrounding the organ by multiplying ---

Q. Let me put it into simple numbers so that I am sure I am following you. If the measured concentration in the Klotz solution was 5, 5 nanograms per millilitre, and if there were 100 millilitres, then I could say in the Klotz solution there are 500 nanograms of digoxin?

A. That is correct, digoxin and/or



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digoxinlike substances, that's right.

Q. So, I could calculate the total amount that was in the Klotz solution, yes, then what?

A. And then I considered that this amount was diffused into the Klotz solution from the heart that was placed, from the fresh heart that was placed in the Klotz solution.

Q. Yes.

A. And dividing this number by the weight of the fresh heart at autopsy I would get a concentration per gram of the fresh heart.

Q. So, you need to know the weight of the heart?

A. That's right.

Q. And you divide that, in grams, you divide that into the total nanograms in the Klotz solution and you arrive at a number of nanograms per gram?

A. Of the fresh heart tissue.

Q. Yes.

A. That's right.

Q. And then what do you do?

A. To that of course I have to add whatever digoxinlike substances I found in the fixed tissue.



I.11

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Q Yes.

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A. I have always added the lowest, since I have studied different regions of the fixed tissue, I have always added the lowest concentration that I found in the different regions to that number.

Q Okay, let's apply that one particularly to this sample T6. Are you looking now at the measurement of digoxin or digoxin and/or digoxinlike substances?

A. That's right. Which page are we on again, I'm sorry?

Q Well, we will turn back to page 6 of this report.

A. 6, okay.

Q You found 118 nanograms in the left ventricle?

A. In the left ventricle.

Q 45 in the right atrium and 147 in the septum?

A. That's right. So, I would have added the 45 to that previous number.

Q You would have used the lowest number?

A. The lowest number, that's right.



I.12

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Q. What, and multiplied that by the
number of grams in the fresh heart?

4

A. Well, this is per gram.

5

Q. Oh, that's per gram, yes, all
right, you're right.

6

7

A. And then I have made of course
assumptions, which I stated in my report. The
assumptions that I have stated is that I assumed that
the digoxin and/or digoxinlike substances were derived
from digoxin and the second assumption was that the
weight of heart at autopsy is as was given to
me by reports.

12

13

Q. Yes. Let me be sure I understand
those two steps. Obviously you have to rely on the
report of the weight from the Pathology Department?

14

15

A. That's right.

16

17

Q. But you are assuming that the
digoxinlike substances essentially are digoxin
metabolites, are you?

18

19

A. No, breakdown.

20

Q. Oh, breakdown, all right.

21

A. Breakdown products of digoxin.

22

Q. All right. Okay.

23

A. This was based on all the research,
some of it was shown here in the slides today.

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I.13

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Q. Yes. So, you now have a
calculated number of nanograms per gram from the Klotz
solution?

A. Yes.

Q. And you have an inferred level
of nanograms per gram based upon the lowest concen-
tration that you recorded in the heart?

A. That's right.

Q. All right.

A. And also of course knowing that
the values in Klotz solution that I have used as well
as in the tissue are probably minimal because of the
degradation of digoxin in those mediums.

Q. Yes.

A. For that reason and with those
assumptions I feel that I was able to give an estimate
of the minimal concentration in the heart before it
was fixed.

Q. I take it you make no claims at
all as to the accuracy of that number that you so
calculated?

A. No, it is an estimate and that's
the way I have expressed it. It is an estimate.

-



J/EMT/ak

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Q. You are satisfied that it is
a very conservative estimate?

A. I believe so, yes. I believe
it is very conservative estimate.

Q. So whatever we see - well, okay,
whenever we see that in a report, the estimate of
the concentration prior to fixing the organ, that
is the process that you went through?

A. That is right. And of course
I applied it only to the instances where the heart
was alone, when I received it it was alone in the
Klotz medium surrounding.

Q. Yes.

A. In instances where I received
specimens with let's say mixed organs I have not
attempted this estimate because of the complexity of
the different organs being mixed together.

Q. You don't know the origin of
whatever digoxin may now be in the Klotz solution?

A. I wouldn't know from where they
came, that is right.

Q. I think with that information
one can read and I hope understand more clearly the
reports that you prepared, Mr. Cimbura.

You analyzed samples of blood and



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tissue from a substantial number of children whose deaths are here under enquiry. By my count some 23 or 24, and in some of them, some of those samples, you measured levels which you reported as being within the fatal toxic range?

7

A. Fatal range as I have expressed it.

8

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Q. Yes, fatal range, a level of concentration which on the basis of your knowledge of the literature was consistent with death resulting from that drug; is that so?

12

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A. Well, in blood, in blood or serum.

14

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Q. Your greatest confidence is with respect to blood, obviously?

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A. Yes. The fatal range in blood is much more significant to me as a toxicologist than the fatal range in other tissues.

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Q. I want to be clear: you are not saying, I take it, Mr. Cimbura, and you don't pretend to say that digoxin toxicity killed any of these children. You can't say that?

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A. Well, the establishment of cause of death is a function of a pathologist.

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Q. Yes.



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A. In my view some of these findings if they were in that fatal range for blood or serum could result in death. They could account for death, that is right.

Q. And if I read your report correctly and you must help me, you made such findings with respect first to Justin Cook. That is set out in the report of January the 11th, and we were looking at the notes a few moments ago. Page 4 really at the top of the page. With respect to blood analyses, serum analysis, and also with respect to the fixed heart - sorry, not fixed heart muscle but fresh heart muscle, you reported your findings as being within the reported range of concentrations in cases of fatal poisoning?

A. That is right.

Q. Similarly with respect to the fresh lung sample, Note 4, you made the same comment?

A. That is correct.

Q. Are there other children with respect to whom your findings were similarly reported? Could you help me with that?

A. Well, I believe Pacsai.

Q. All right. And the notes that are found on page 5, where you report:



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"The concentration of digoxin in the serum is within the range of values reported in blood or serum from cases of fatal poisoning."

A. That is correct. As I remember in addition to that there was some more items received from Pacsai, from the child Pacsai.

Q. Yes.

A. And there are also in my reports issued on March 25th and September 29th.

Q. All right. September 29th, Exhibit 95E, and March 25th is Exhibit 95C.

Could we look at 95C first? March 25th. And there on page 2. Certain reports with respect to samples from Baby Pacsai. Are those the matters to which you refer?

A. Yes. This is one report. There is a second report as well, another report, that is right.

Q. Exhibit 95E is the report of September 29th, and you referred to that one and there on page 5. The lower half of the page there is a report on Sample T104, sample of tissue in foil marked with an autopsy number, lung, where you say:



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"The tissue was found to contain 122
nanograms per gram of digoxin."

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And you say "that concentration is inconclusive with
respect to toxicity".

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A. Yes. It is by itself, that
is right. If it was by itself.

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Q. Yes.

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A. But it is above the range that
is known for normal.

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Q. All right.

11

A. For children receiving normal
digoxin.

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Q. It is above the reported
therapeutic level.

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A. For lung tissue, that is
right.

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Q. By itself it would be incon-
clusive, but I take it you read that in conjunction
with the serum level which you measured and reported
to be in the fatal range?

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A. That is right. It provides me
with supportive information with respect to the
first - with respect to the finding in the serum,
that is right.

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Q. All right. On page 6 of your

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first report, January 11th, 1982, Mr. Cimbura, at the top of the page, the notes on the samples assayed from Allana Miller, you report:

"The serum concentration of digoxin is 69 nanograms per millilitre, within the range of values reported in blood or serum from cases of fatal poisoning."

A. That is correct, sir.

Q. That therefore is the third child in whom you found a sample in which you measured a level of what you considered to be digoxin within the reported range of fatal concentrations?

A. That is correct, sir.

Q. Was there any other child?

A. The child Inwood.

Q. In the case of Inwood - I'm trying to find the reference. T26, page 8. Page 8 of the very first report, Mr. Cimbura, I believe.

You are thinking of the serum, the blood sample, are you?

A. Well, from the child Inwood there was what I presume to be a serum.

Q. Yes.

A. This is I believe in my report.

Q. March 25.



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A. Either March 25 or September 29.

Q. March 25, Exhibit 95C I think. "The following specimen is reported to be from Kristin Inwood. Small sample of brownish fluid in vial bearing seal number...Labelled Inwood, K, reported to be serum."

And the result:

"The serum was found to contain 491 nanograms per millilitre of digoxin."

A. That is correct, sir.

Q. And your note:

"The concentration of digoxin is above the range of values reported in blood or serum from cases of fatal poisoning."

With respect to that sample,

Mr. Cimbura, did you subsequently discover that it had a rather odd history?

A. Well, it was reported to me - of course this sample was received very late at the Centre. I don't know the timings now --

Q. It was reported as received January 28th, 1982.

A. That is right. So it was



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received some time after the child died, and it was reported to me that as part of the storage at the Hospital the sample was subjected to heating for a period of time at a certain temperature.

Q. Yes.

A. That is what you are referring to?

Q. Yes, indeed.

A. That is right.

Q. And did the fact that the sample had been subjected to heating at a certain temperature for a certain time give you any cause for concern about the reliability of the result you recorded in the sample?

A. Well, it was something that I felt we should simulate an experiment and we have used serum, one of the serums from the manufacturer as I mentioned before, and we have simulated the temperature and the heating of the serum which was targeted to contain 2 nanograms per millilitre.

The results obtained were not significant. There was no change before and after heating which would indicate to me that this particular heating treatment may not have affected the serum to a very large extent.



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J9

Q. Mr. Cimbura, one thing does puzzle me about it, though. Could you turn to your very first report of January 11th, 1982.

A. Yes, sir.

Q. Pages 7 to 8.

On page 7 you set out the reports of the analysis of Sample T8, heart of Kristin Inwood. At the top of page 8 you complete that report, and then go on to T26,

"Sample of yellowish fluid in tube bearing seal number...Labelled 'Inwood, Kristin'."

A. Yes.

Q. And there the report is "no digoxin could be detected".

A. That is correct, sir.

Q. Did the coincidence of two reports on what is allegedly blood from this same child, one in which no digoxin could be detected and the other in which you record a level of 491 nanograms per millilitre cause you any concern?

A. Well, the information that I had is that the sample, the serum, my Item T26 --

Q. Yes.

A. -- was obtained ante mortem



J10

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before death from the child Inwood.

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Q. From whom did you get that

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information?

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A. Well, for one thing it was

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labelled, described on my report at 12-3 there was
part of a labelling.

7

Q. Oh, yes.

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A. Which I presume to be the

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12th of March, and I do not recall now when the
child died.

10

11

Q. I see. But if your information

12

be correct the sample of blood drawn from the child

13

on March 12th did not contain digoxin?

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A. That we could detect.

15

Q. That you could detect.

16

A. That is right.

17

Q. Higher than 2 nanograms, but

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the sample which you reported on March 25th --

19

A. Obtained post mortem.

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Q. Which was obtained post mortem

21

and yielded a level of 491 nanograms per millilitre.

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A. That is correct.

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Q. Now with respect to Inwood

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and recognizing the reservations you have about

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results found in fixed tissue, could we look at page 7



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of the first report. Beginning on the lower half of the page, Sample T8, heart Kristin Inwood, which you have analyzed as the left ventricle, left atrium and septum and to the Klotz fixative, can you tell me whether you attach any significance to the levels reported there in that heart tissue in light of the blood reading of 491 nanograms? Did the 491 nanogram reading do anything to overcome the reservations you had about relying upon fixed tissue levels?

A. I should mention that with respect to this child the values that are found in the fixed heart of this child were the highest values found in all the cases I have examined. My estimated - from this data, my estimated minimal concentrations in her fresh heart was not less than 549 nanograms per gram.

Q. And so stated on page 8 of your note?

A. So stated on page 8. Which is within the therapeutic range but above the average therapeutic range.

Q. Above the average or about the average?

A. Above.



J12

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Q. Above the average?

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A. Above the average for heart

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tissue, yes.

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Q. Is it also within the range

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of concentrations that have been recorded in the

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case of fatal poisoning?

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It is, yes. So that all by itself
I consider the value in Klotz medium as inconclusive.

Q. Yes.

A. In combination with the high
volume that I found in the presumably postmortem serum
and I considered that as supportive evidence.

MR. LAMEK: Excuse me a moment, please.

Now we have done then I believe four
children in whom you recorded levels that you note
as being within the fatal range as reported in the
literature?

A. Within or above.

Q. I am sorry?

A. Within or above fatal.

Q. Within or above, yes. That
is to say Cook, Pacsai, Miller and Inwood. Are there
any other children that you can recall, and I tell
you I haven't seen any on my reading of your report,
in whom you found a level which was so described.

A. I cannot recall.

Q. And I take it, Mr. Cimbura,
that you are reluctant to regard as conclusive levels
found in fixed tissues alone?

A. That is correct, sir.

Q. And even more reluctant to



1
2 attach significance to any levels found in exhumed
3 tissues?

4 A. By themselves, that is right.
5 The significance with respect to toxicity of course
6 in some of these infants, the significance of just
7 the qualitative findings was important, but with
8 respect to the toxicity yes, that would be generally
9 correct I think, that's right.

10 Q. You did report findings of
11 digoxin from which I inferred that the samples were
12 subjected to HPLC as well as RIA?

13 A. That is correct.

14 Q. In the cases of Hines,
15 Lombardo and Belanger?

16 A. That is right, sir.
17 Actually Lombardo and Belanger in addition to RIA
18 and HPLC other tests have been done as well.

19 Q. That is the one thing I wanted
20 to ask you before leaving this matter of your results.
21 You told us when you were last here that you did
22 yours, I think at that time you said in one case,
23 you got a positive result in one case with the use
24 of mass spectrometry, and gas chromatography. Can
25 you tell us please the extent to which you attempted
to use those techniques to identify digoxin in these



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samples?

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A. I am not sure I understand the question. The extent ---?

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Q. Yes, how many samples did you attempt to use those techniques?

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A. Well we have attempted to use, we have used it on the child of Lombardo, and then we have also used it on the examination of the Klotz fluids surrounding the fixed heart of the child Warner. We have also used it in the examination of specimens from the child Belanger.

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Q. Is there any reason why you did not seek to make more extensive use of gc and mass spec.?

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A. It is essentially a technique which is not as readily applicable to the analysis of digoxin in postmortem materials as are other techniques that we have used, that is it has disadvantages for example in point of view of sensitivity of detection, a very big disadvantage from that point of view. So it really couldn't be used routinely from that point of view because you just would need a much higher concentration to study and it is a much more complex instrumentation also.

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MR. LAMEK: May I ask you to bear with

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me for just a moment, Mr. Cimbura, please.

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THE COMMISSIONER: Would this be a good

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time?

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MR. LAMEK: Indeed I think it would,

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Mr. Commissioner. I have finished with the results

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and I am going into another area anyway.

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THE COMMISSIONER: All right.

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Depending on whether Mr. Lamek has any further

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questions, Mr. Hunt, you will be first up and second

last up on this witness.

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MR. HUNT: Thank you, Mr. Commissioner.

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THE COMMISSIONER: Yes, all right

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until 2:30 then.

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---Luncheon recess.

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--- Upon resuming at 2:30 p.m.

THE COMMISSIONER: Yes, Mr. Lamek?

MR. LAMEK: Thank you, sir.

Q Mr. Cimbura, when we broke for lunch I was promising to move to the final area of my questions relating to the other studies of which you have provided me with summaries. Just before I do that, just two questions very briefly about the first area of your evidence this morning.

You mentioned on more than one occasion that the lower limit of detection on your RIA equipment was 1 nanogram; do you remember telling me that?

A With respect to blood.

Q With respect to blood, yes, I take it that is a limit which you yourself determined in the calibration of the equipment?

A Well, that is the limit which we designed the procedure to have that limit.

Q Yes.

A That's right.

Q Are you not interested in any reading less than 1 nanogram?

A Well, not really remarkably. At that stage when I designed it I wasn't really



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interested, you know, with any great, relatively great curiosity about levels below 1, no, because these are very low levels.

Q. For toxicological purposes I take it a level less than 1 is not of great significance to you, is that the reason?

A. Well, it could be sometimes of significance, but not of great significance usually, that's right.

Q. Whereas in a clinical setting it may be important to have measurements below that level?

A. That is right, yes, this was one consideration. Another consideration of course was that in the design of the procedure a balance has to be established between - from analytical considerations as to what limit of detection to set.

Q. Yes.

A. Because by setting it too low you may encounter difficulties with, let's say, some substances which may cross react at the lower level of the RIA standard curve.

Q. And what is the upper limit of the standard curve on your equipment?

A. Well, on our procedure the



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standard curve is expressed actually from 50 to 600
picograms, that is about 0.1 millilitres.

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Q. Now you are confusing us,
Mr. Cimbura, that is unfair, what is a picogram?

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A. A picogram is one-thousandth
of a nanogram.

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Q. A thousandth of a nanogram?

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A. That is right, and it is not
meant to be confusing really.

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THE COMMISSIONER: A thousandth of a
nanogram, what was the number of these strange ---

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THE WITNESS: 50 to 600 picograms.

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THE COMMISSIONER: 50 to 600.

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Q. For what unit of liquid?

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A. 0.1 per ml. of the sample
analyzed.

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Q. So it is one-thousandth of a
nanogram to one-hundredth of a millilitre?

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A. It is, one picogram is a
thousandth of a nanogram.

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Q. 0.12 of a millilitre is one-
hundredth of a millilitre?

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A. Is one-tenth of a millilitre.

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Q. Oh, 0.1, all right, yes. I am
almost sorry I asked Mr. Cimbura, I knew it was a bad

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idea. I was really interested in why you had to come up with 1. I take it you have no difficulty in translating from your curve to the nanogram per millilitre, your results are expressed in those terms, are they not?

A. That is right, it is a question of mathematical calculations.

Q. And the other thing was in the various data of which we looked at summaries this morning, you were unable to tell me with any particularity just when a particular study may have been done, or begun, or completed. Can you give me the overall period in which those data were accumulated, the ones that we looked at this morning?

A. Well, without referring to more details, as I recall it some would start as early as April, May, 1981; and again as I recall it some were I know as late as August, 1982. There may have been some even later than that, but that is roughly the period.

Q. Depending upon the purpose for which you were accumulating the information I take it?

A. That was one of the reasons, that's right, yes.

Q. Now when we come to this final



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area as I now do, Mr. Cimbura, I understand that in the course of establishing the procedure for the RIA and for the HPLC, and in the course of preparing yourself to have an appreciation of what you might find and preparing yourself to conduct the analysis, you also undertook other studies in addition to those that we referred to this morning, other studies and research projects which may be of interest and assistance here and I want to ask you about those if I may.

In the bundle which we marked as Exhibit 213 this morning, the next document, or summary, is headed: "Postmortem Blood Digoxin Concentrations of 33 Control Children on Digoxin Therapy".

Do you have that document, Mr. Cimbura?

A. Yes, I have it, sir.

Q. Can you tell me more or less approximately when in the process of your work this study was done?

A. Well, this study was continuing, sir. It was a study that was begun in some aspects as early as the period I mentioned, some time in late spring of 1981 and was continuous in the sense that we were - it was kept up until late 1982.



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Q. I know you said when you first gave evidence here, Mr. Cimbura, that with respect to postmortem blood samples you would be interested in knowing the site from which the sample was drawn?

A. That is correct, sir.

Q. And I take it that this study was designed to establish whether there was any difference to be detected in the levels to be expected in blood from different sites in the body, postmortem blood?

A. This was one purpose of the study, that's right.

Q. What were the other purposes?

A. Well, the other purposes obviously would be to find the extent of the levels in post-mortem blood from children.

Q. I am sorry?

A. On normal therapy.

Q. Yes, on normal therapy. Now as I understand it here your total population or children was 33?

A. That is correct, sir.

Q. And from those 33 children you obtained in the first place samples of blood from various sites, and without differentiation you have



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recorded the range of digoxin measurements made in
those samples, have you not?

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A. That is correct, sir.

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Q. On the first line under the
headings there?

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A. That is correct.

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Q. And those measurements range
from negative to 12.4 nanograms per millilitre?

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A. That is correct, sir.

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Q. And then in the case of 18 of
the children you obtained samples of heart blood
post mortem?

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A. Yes, I was given, I obtained
this, yes.

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Q. These all came from The Hospital
for Sick Children I take it?

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A. Certainly the vast majority,
probably all of them, probably, yes.

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Q. And in each case you have
indicated the range of ages of these children, and
you have noted the interval between death and autopsy,
and autopsy I take it was the time at which these
samples were obtained. You have recorded again that
the range of measurements there is again negative
to 12.4 nanograms?

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A. That is correct, sir.

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Q. I notice that 12.4 nanograms has a footnote, Footnote 5, which records that - in the first place that was the only measurement that you made greater than 10 nanograms in any of the samples from these children?

A. That is correct, sir.

Q. And that the last dose which was given intramuscularly was given two and a half hours before death?

A. That is correct, sir.

Q. And do you attach any significance to the fact that the dose is given two and a half hours before death?

A. Well, I thought it would be interesting since this was my highest level that I have achieved. Of course I was interested in the circumstances of the dose and so on, and I have found this information and I have noted it. I noted that it was given by intramuscular injection.



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A. I haven't been able to find too much literature to tell me when the peak occurs after intramuscular injection. So, I mainly noted the information down so it is not forgotten.

Q. You have noted it and perhaps it is something that the pharmacologists can help us with?

A. That's right, yes.

Q. Yes. Is that 12.4 result the same one that is recorded in the top line under various sites, is that the same sample?

A. That's the same child, that's right.

Q. Same child, same sample?

A. That's right.

Q. And was that the only result of all the samples that you assayed for this study which was over 10?

A. Of the 33 children that I had studied, that is right, those were the only over 10, that's right.

Q. And then finally you obtained 27 samples of sagittal sinus blood from among these 33 children. Some of the older ones didn't supply samples of sagittal sinus blood, I take it it is a



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little hard to get at, sagittal sinus, in older children. You recorded levels there between negative and 9.7 nanograms?

A. That is correct.

Q. But again you record in Footnote 6 that there was only one level of those 27 higher than 7 nanograms?

A. That is correct, sir.

Q. All right. And you have noted the report that you received about that child's renal condition?

A. That is correct, sir.

Q. Now, we will come later I know, Mr. Cimbura, to the detailed listing of the 18 heart blood samples, that is the subject matter of a separate summary, is it not?

A. That is correct, sir.

Q. One can see the ranges there. But was it on the basis of, among other things, this information that you were able to record from your own research the ranges of therapeutic - I'm sorry, the ranges of digoxin concentrations in postmortem blood from therapeutic dosages that were referred to in your reports?

A. That is correct, sir.



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Q. And that was of assistance to you for that purpose?

A. That is correct, sir.

Q. Thank you. Next, Mr. Cimbura, you did a study entitled "Digoxin Concentrations in Heart Tissue", of 13 children, control children on digoxin therapy. These, as you have noted, are children who died from causes other than digoxin poisoning?

A. Yes.

Q. And you have noted the number of patients from whom you received samples of particular kinds of heart tissue, their ages and the ranges which you obtained on assay.

What conclusions or inferences if any were you or are you able to draw from that study as it is summarized on this document, Mr. Cimbura?

A. Well, the first conclusion is that the therapeutic range in children, as is indicated by my research, ranges between 49 nanograms per gram and 383 nanograms per gram when studied in ventricles or septum regions of the heart.

I have also divided the ventricle study into children of ages more than one month and less than one month.



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Q. Yes.

A. And the results indicate that older children tend to have higher concentrations in the regions of the heart than younger children, which is consistent with the reports described in the literature.

Q. I'm sorry, I am reading this wrong then. It would seem to me that the older children have lower concentrations.

A. That's right, isn't that what I said?

Q. I'm sorry, I thought you said higher.

A. Oh, I'm sorry.

Q. Maybe I just didn't hear you. Children under one month seem to display levels after therapeutic treatment that are higher than those of children over one month?

A. That is correct, sir.

Q. Yes.

A. And that illustrates the point which we all have learned to recognize in interpretations of digoxin concentrations in the children under investigation that age is a very important criteria to consider.



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Q. Yes. Is the study sample large enough for you to be able to draw that conclusion, Mr. Cimbura?

A. Well, as I mentioned, Mr. Lamek, the results show it and it is consistent with the results reported by the literature. The sample number is not very large, that's all I could do.

Q. All right. But it is consistent with the reports in the literature?

A. That is right.

Q. Yes. Next, Mr. Cimbura, you have provided a summary of digoxin concentrations in postmortem lung tissue and blood. Here there were four control children on digoxin therapy ranging in age from two days to eight and a half months. You have recorded the interval between death and post mortem and the interval between last dose and death and have noted the levels recorded in sagittal sinus blood and in lung tissue?

A. That is correct, sir.

Q. Now, again, I ask you is there any reason for that rather small sample size, for children?

A. Well, I would have liked to



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have received a greater sample size but this was the only sample size that I was able to receive. It does illustrate a range that one could expect in this, as you said, a rather small sample size studied.

Q. Is the sample large enough to draw any valid conclusions or inferences from?

A. Well, it depends what kinds of conclusions I suppose, Mr. Lamek.

Q. Yes. How about useful ones?

A. I believe I mentioned before that by themselves tissue levels, I do not really consider by themselves conclusive with respect to digoxin toxicity.

Q. Yes. Certainly you said that with respect to fixed tissue levels. Do you take the same position with fresh tissue levels?

A. Unless they are extremely - unless the values are of very extreme proportions.

Q. All right.

A. I would consider that also for fresh tissue levels by themselves.

Q. Yes.

A. Unless I had some other findings to support them.

Q. Okay. Is there anything in the



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literature of which you are aware which indicates that the ranges of levels that you were recording in this study may indeed be representative of the ranges that you should expect to find in sagittal sinus blood and lung tissue in children of this age?

A. Well, from the literature - the ranges in where, in lung tissue did you say?

Q. In lung and sagittal sinus blood.

A. Well, sagittal sinus I don't recall being studied in the literature. I don't recall and I am not aware of any papers in the literature. The heart blood, the upper maximum limit is 12.4 in infants. I recall only one published literature report where the level in postmortem blood was stated to be 15 and this was from an adult person.

Q. All right.

A. And as far as unpublished literature or reports I believe the Hastreiter group told me that they may have found it somewhat higher in some children but it hasn't been published, I haven't seen it yet.

Q. Well, we will hear from Dr. Hastreiter about that perhaps.



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A . Right.

Q. Mr. Cimbura, the next document consists of only two samples, as I understand it. It was an investigation of the stability of digoxin in postmortem blood specimens. I take it just as you have tried to establish whether digoxin was stable in - we have seen Klotz solution and embalming fluid, so, you are interested to know what happened to it in postmortem blood if the samples stood for a period of time, were you?

A. Yes, I was interested, that's right.

Q. And you let these two samples stand for, what, some 18 months?

A. Between June, '81 and January, '83 which, yes, it's about 18 months, something like that.

Q. Now, is there any reason why this study was restricted to two samples?

A. I suppose when I have thought of this study and when it was set in motion I am not sure whether we could find any more of the bloods that we had that old to compare, you know, on subsequent analyses. I'm sure that we looked through more. But that may be one reason.



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Q. Well, Mr. Cimbura, whether or not one can generalize on the basis of the results that you did have, it appears in the one case that over the space of 18 months the second level appears to be a reduction of some 25 per cent approximately from the first level, 4.5 down to 3.4 and the second drop from 1.6 to 1.4.

With respect to that second sample, is the difference between the two assay results within the anticipated degree of interassay variation?

A. For the second sample?

Q. For the second sample.

A. Yes, I would think so, yes.

Q. So, we can't take any kind of necessary decline from that second result I take it, 1.6 to 1.4?

A. That is correct.

Q. It may or it may not indicate an absolute decline in digoxin present?

A. It may or may not. I considered that an analytical variation, possibly.

Q. Do you attach any significance to the decline of approximately 25 per cent in the concentration in the first sample from 4.5 to 3.4?

A. Well, you mentioned it is



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25 per cent, I haven't done that.

Q. Approximately 1.1 over 4.5,
that is about 25 per cent.

A. For a sample of this concentra-
tion I would normally expect less variation.

Q. All right.

A. But however regrettably it is
only one specimen.

Q. Mr. Cimbura, may I ask you
this in the context of something that arose yesterday
and the day before.

If there remain any remnants of
the samples of blood which was supplied to you via
the police for the purpose of this work that you are
reporting today, if any remnants still remain of
those samples, do you have any opinion as to the
likelihood, if they were now to be reassayed using
your own procedure, for example, whether the results
today would be consistent with the results that you
achieved two, two and a half years ago? Would the
samples - do you have any basis for knowing whether
the samples would yield approximately the same
results now as they did then?

A. I have no factual basis, we
haven't done that comparison.



Cimbura, dr.ex.
(Lamek)

BB11

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Q. All right. They may or may not.

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A. Yes, that's right.

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Q. All right. I take it you do

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not have sufficient information to be able to

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predict with any confidence what happens to digoxin

7

concentrations in postmortem blood over an extended

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period of time?

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A. Well, I haven't done any

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experimental research on that, but for example, the

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tissues and embalming fluids and in Klotz, as I have

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attempted to illustrate this morning, are subject

to degradation over time.

13

Q. Yes.

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A. So, there one would expect

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even further degradation.

16

Q. Although it does not appear to

17

be quite so dramatic from the document that we have

18

just looked at to the extent that you can draw any

conclusions at all.

19

A. This is not a preserved blood

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now.

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Q. No, no, I am talking about

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blood only.

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A. Oh, blood, I'm sorry.

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Q. If there are remnants of the

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blood samples still left do you have any way of knowing whether, if assayed today by you the results would be consistent with ones you achieved two years ago?

A. I haven't done it.

Q. Fine.

A. They may be.

Q. They may be or they may not be, all right.

Now, there are just a couple more documents, Mr. Cimbura, if I may.

Your next document is entitled "Regional Distribution of Digoxin in Brain Tissue of 8 Control Children on Digoxin Therapy". Now, when and why did you do this study, Mr. Cimbura?

A. Yes, this study was carried out because one of the exhumed children - a brain was provided for examination and the reason for that was about that time, or slightly before that time there was a literature report from a group in California where suggestions were made that analysis of certain regions of brain for digoxin may provide useful diagnostic information with respect to toxicity.



1
2 This was the reason why this study was began.

3 Q. All right. The purpose I
4 take it, Mr. Cimbura, was to let you know the kind
5 of numbers you might expect to see in children on
6 normal digoxin therapy from different regions of the
7 brain?

8 A. That is right, yes.

9 Q. Were the results that you
10 achieved consistent with those reported in the
11 literature in terms of relative distribution?

12 A. The results that I have
13 achieved have enabled me, Mr. Lamek, to reach a
14 conclusion that the brain concentration in the child
15 that I was supposed to - that I was given to examine,
16 that I considered inconclusive in respect to digoxin
17 toxicity.

18 In some aspects it does agree with the
19 literature; in some it apparently does not because
20 the literature reference was done on adult patients,
21 and as I have mentioned previously the age difference
22 is an important difference.

23 Q. Yes.

24 A. For digoxin. And I believe
25 it constitutes a first study on digoxin therapeutic
concentrations on infants in the regions of the brain.

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Q. I take it it prevented you from
relying to too great an extent upon the literature
report because in some respects ---

A. That is right.

Q. - you say your results were
inconclusive?

A. That is right. I felt I had
an obligation to follow the literature report, but
research - results of my work enabled me to reach
a conclusion that the results that I obtained are
inconclusive in respect to digoxin toxicity.

Q. Yes. Now the next document is
a two-page one, Mr. Cimbura, the second one being
the note and key, but this one I think to be of some
significance and is entitled "Distribution of
digoxin postmortem blood from different sites and in
vitreous humour of 18 control children on digoxin
therapy".

Vitreous humour is taken from the
eyes, isn't it?

A. That is correct, sir.

Q. And sites which you examined
here were heart, sagittal sinus, femoral vein,
subclavian vein and the iliac vein?

A. The iliac vein, that is right.



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Q. Right. So far as the heart column is concerned, those I take it are the 18 children whose postmortem heart blood levels were summarized in a document we have already looked at?

A. That is correct, sir.

Q. These were the ones that ranged up to a high of 12.4?

A. That is correct.

Q. The second sample is the one that showed the 12.4, the next highest being No. 9 at 9.9?

A. The 9.7, is it?

Q. 9.9 is No. 9 and after that we drop down to 8.1.

A. We are under sagittal sinus now?

Q. No, I am under heart.

A. Oh, okay.

Q. Those are the 18 children we have already seen summarized elsewhere, are they not?

A. That is right.

Q. Now when we get to FV1 and FV2, those are the femoral veins as I understand it?

A. That is correct, sir.



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Q. Now we have heard from Dr.

3

Mancer that at one point he and you devised a protocol

4

for the drawing of blood samples which as we under-

5

stood it from him were designed to duplicate the

6

manner in which samples were drawn from Baby Estrella?

7

A. As I understand it that is

8

right, sir.

9

Q. And there was a sagittal sinus -

10

I am sorry, there was a gutter blood sample, and a

11

protocol was established to obtain similar samples

12

from other children. And at the same time the

13

protocol was established for the obtaining of samples

14

from leg vein which I take it in this case he

designated as the femoral vein?

15

A. That is correct, sir.

16

Q. And the protocol called for

17

obtaining a sample from the leg vein at the beginning

18

of the autopsy and then three hours later?

19

A. Approximately three hours

20

later, that is right.

21

Q. And I take it the object of

22

the exercise was really to accumulate data to help

23

you to assess the significance or reliability of

24

the Estrella results in the samples in which they had

25

been found?



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A. That was the first purpose,
that is right, yes.

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Q. Yes.

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A. Other purposes was to study
the distribution and so on.

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Q. Yes. Thank you.

8

Now, Mr. Cimbura, do you recall when
it was that you and Dr. Mancer got together to
design that protocol?

10

A. I have some of our documents
with the date on it. I don't remember the exact date.

11

12

Q. Right.

13

A. I know it was after the
preliminary hearing.

14

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Q. All right. When did you first
become aware that there might be some question about
the propriety or the integrity of the Estrella
sample in which a level of 72 had been recorded in
the Hospital?

18

19

A. As I recall it this was after
the preliminary hearing, and pursuant to a phone call
to me by Dr. Mancer.

20

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Q. All right. And it was there-
after that you and he got together and prepared a
protocol and started collecting those samples for

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a study?

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A. That is correct.

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Q. And was it in your lab that

these samples were done that were collected?

5

A. That is right.

6

Q. Samples were collected at the

7

Hospital in the Pathology Department and sent to you

8

for assay?

9

A. That is correct.

10

Q. And are the numbers which appear

11

under the Columns FV1 and FV2 in the document in which

12

we are now looking the results of your assays of the

13

leg vein samples drawn in accordance, as you understood it, with that protocol?

14

A. That is correct, sir.

15

Q. All right. Do you have any

16

comment to make upon the samples that were so

17

obtained and analysed, Mr. Cimbura?

18

A. Well, the results of this

19

research substantiated my opinion that blood drawn

20

from heart post mortem tends to give the highest -
higher results than ---

21

Q. Yes.

22

A. - than blood drawn from a

23

sagittal sinus vein.

24

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2 Q. Could I ask you to focus on
3 the femoral vein results? Do they provide you with
4 any basis for considering that the sampling technique
5 which was used in Estrella, although not perhaps
6 ideal, distorts the results in terms of digoxin
7 assay? Is there any basis for questioning the
8 appropriateness of the sample and of the result
9 achieved in it?

10 A. No. They tend to be lower,
11 as I would expect it from the femoral vein. It is
12 a peripheral circulation, and there were suggestions
13 to this in the literature and this is the results I
14 expected to get it would be lower than anywhere else.

15 Q. Indeed there are only four
16 positive results recorded under the FV2 column. As
17 I read the attached key FV2 was the sample drawn three
18 hours after the beginning of autopsy?

19 A. That is correct.

20 Q. And therefore the one which
21 in fact most closely approximated the timing of the
22 Estrella sample. And those values appear, do they
23 not, to be slightly lower than those recorded in the
24 FV1 sample?

25 A. Yes.

Q. Now other than as you said



1
2 that generally the heart levels are higher than those
3 found - heart blood levels are higher than those find
4 in the sagittal sinus blood and the comments you have
5 made on the FV samples, are there any other con-
6 clusions or inferences that you would draw from the
7 data recorded on this sheet, Mr. Cimbura?

8
9 A. Well, I think the results in
10 the vitreous humour are interesting from the point of
11 view that at least one child which was under
12 investigation, and I believe the child was the child
13 Miller, vitreous humour value was obtained on that
14 child, and comparing it to the results of my research
15 the value found on the child Miller is above the
16 range that I found in these normal - children on
17 normal therapy.

18 Q. You found a value as high as
19 2.6 in patient No. 18 or child No. 18?

20 A. That is right.

21 Another aspect of interest was the
22 controversy in the literature about the significance
23 that might be attached to a circumstance when vitreous
24 is lower than blood.

25 Q. Yes.

A. The controversy in the
literature reports existed to that effect in a sense



1
2 that some authors felt that if the vitreous level
3 is lower, much lower than blood, it might imply that
4 the interval between last dose and death was relatively
5 short.

6 Q. Yes.

7 A. And other body of research
8 in literature concluded that this was not true, so
9 there was a controversy on this aspect.

10 My results tend to indicate that
11 you really cannot make conclusive opinion because
12 even after 19 hours such as in Case No. 10 ---

13 Q. Yes.

14 A. - the vitreous level is
15 still considerably lower than blood.

16 Q. Yes.

17 A. And only after 66 hours in
18 Case No. 18 does the vitreous level approach some
19 sort of equilibration with the blood.

20 Q. Yes.

21 A. So that really for practical
22 means of giving a clue to the investigation of these
23 cases I don't think that any conclusion can be drawn
24 in this aspect from the vitreous humour.

25 Q. In that regard what your
research made clear was that it was not very clear?



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A. That is right.

Q. And then we come to the piece of paper, Mr. Cimbura, that summarizes the result of the gutter blood study. Headed "Comparison of Digoxin Concentrations of Postmortem Blood and Fluid from Pelvic Cavity from 14 Control Children on Digoxin Therapy".

Once again with these 14 children you have recorded levels in sagittal sinus blood and heart blood, and then two values for the pelvic cavity or gutter blood: one from samples drawn at the start of autopsy and a second three hours later. And the number that obviously stands up like Mount Everest in the whole thing is No. 5 at the start of autopsy, a level of 169.6.

Other than that sample 5, Mr. Cimbura, do you make any comment on the levels achieved in the samples of gutter blood or pelvic cavity blood shown on this document?

A. Other than this Case No. 5 the concentration in the gutter blood, or perhaps pelvic cavity is a better word.

Q. Yes.

A. Were below the upper range of my values for children on normal therapeutic digoxin.



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In other words they were below 12.4.

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Q. They were within what you
had established by your experiments to be a range
for children on therapeutic digoxin doses?

5

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A. That is right.

6

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Q. And the only one that stands
out is No. 5?

8

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Can you tell me when and at whose
suggestion this study was undertaken into the gutter
blood or pelvic cavity blood sample?

10

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A. Well, I believe following Dr.
Mancer's phone call to me I may have suggested it,
that we start some research to get a more definitive
answer.

14

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Q. Other than speculation in
which, of course, we are not interested, Mr. Cimbura,
and I know you are not, other than speculation do
you have any explanation for the apparently anomolous
result in Case No. 5?

19

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A. Well, it is obviously not
normal results because we have true blood comparison
in that case.

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Q. Yes.

A. So it is obviously an abnormal
artificially elevated false result which could be



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produced by not a normal procedure - due to something like contamination.

Q. Well, can we say anything more than this, Mr. Cimbura, that Sample No. 5 or Case No. 5 at least indicates that blood from the pelvic cavity may yield a very high level which is not consistent with the levels found in blood elsewhere in the body?

A. That is correct, sir.

Q. All right.

A. And since it is only 1 out of 14 I would say may with low level - small possibility.

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Q. A small possibility that
it may?

A. That is correct.

Q. Now, we know that the
Estrella level of 72 was obtained from a sample
drawn from the pelvic cavity. In light of your
research and the numbers that are produced on this
document, would you, as a toxicologist, dismiss
the 72 level as meaningless in light of the source
from which it came?

A. No, I would not dismiss
it entirely. No.

Q. I take it, though, in
light of Case No. 5, you could not place total
confidence in it?

A. I could not place as
much confidence in it as if the blood had been
drawn from an intact vein.

Q. Thank you.

Mr. Cimbura, I have one more
document about which I would like to speak to you
or at least have you identify it.

It is, as I understand it, a
table of the times at which the various substances
which you are separating by HPLC come off the Column.



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I think Mr. Scott asked you about
that in the course of your examination last time.

A. That is right.

Q. Have I correctly identified
this?

A. That is correct, sir.

MR. LAMEK: Thank you.

May that be the next exhibit,
please, Mr. Commissioner?

THE COMMISSIONER: Exhibit 215.

--- EXHIBIT NO. 215: HPLC Behaviour of Digoxin,
Metabolites and some other
drugs, Table 1.

MR. LAMEK: Q. Do I take it,
Mr. Cimbura, that this is a complete list of the
substances which you attempted to separate out of
your sample by HPLC for digoxin assay purposes?

A. Yes, to the best of my
knowledge.

Q. And that, in the Column
Retention Time in Minutes, does that indicate the
time after the Column, after the process has begun,
that the various substances come off the Column?

A. This indicates the peak
at which they are routed from the Column, that's
right.

Q. And what is the meaning



DD3

1 of an asterisk under the Column Retention Time?

2 A. That states, of course,
3 that the substance does not elute within twenty
4 minutes of injection, meaning that the analyst
5 waited for twenty minutes and, since it didn't
6 come out, he just didn't consider it significant
7 to wait maybe another hour or another two hours,
8 whatever time it may take to come out of the column.

9 Q. I take it, by then, the
10 digoxin in which you are interested, in any event,
11 had already come off the Column?

12 A. Yes. The digoxin, under
13 these conditions, would come off, as indicated, in
14 nine minutes, that's right.

15 MR. LAMEK: Mr. Cimbura, thank
16 you very much.

17 THE COMMISSIONER: Mr. Hunt.

18 MR. HUNT: I have no questions.
19 thank you.

20 THE COMMISSIONER: Thank you.

21 Mr. Brown.

22 MR. BROWN: I have a few questions
23 but if I might make a request.

24 Mr. Commissioner, would this be
25 an appropriate witness in which the order should be



DD4

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2 slightly changed and that counsel for the Metropolitan
3 Toronto Police precede us?

4 THE COMMISSIONER: He almost
5 escaped!

6 What do you have to say about that,
7 Mr. Young?

8 MR. YOUNG: I'm afraid I must
9 apologize, I didn't hear my friend's comments.

10 THE COMMISSIONER: He wants you
11 to go first into the fray.

12 MR. YOUNG: Well, I can do that.
13 I have no questions of this witness.

14 MR. BROWN: I had a feeling that
15 would be it.

16 CROSS-EXAMINATION BY MR. BROWN:

17 Q. Mr. Cimbura, I act for
18 Nurse Susan Nelles and, right at the end of your
19 testimony this morning, in response to questioning
20 by Mr. Lamek, you said that there was a third test;
21 the mass spectrometry test, which you conducted on,
22 I believe, three children; Baby Lombardo, Baby
23 Warner and Baby Belanger; is that correct?

24 A. That is correct, sir.

25 Q. And Baby Lombardo, I
understand that you previously testified as to the



1
DD5 2 results on Baby Lombardo at the preliminary inquiry
3 into the charges against Nurse Susan Nelles.

4 At that time, I recall that, in
5 response to a question from the Crown Counsel, you
6 described the state of the tissues which you found
7 in Baby Lombardo, and indicated that:

8 "they were smelly and in an
9 advanced state of decomposition;
10 there was no extensive damage and
11 they were not excessively dry."

12 Do you recall that description
13 of the tissues?

14 For your counsel's assistance, I
15 can direct him to Volume 32, pages 3 and 4.

16 THE COMMISSIONER: Whose evidence
17 was that?

18 MR. BROWN: This was the evidence
19 of Mr. Cimbura at the preliminary inquiry.

20 THE COMMISSIONER: Oh, I see.

21 MR. BROWN: Volume 32.

22 THE COMMISSIONER: Perhaps you had
23 better read it to him, because I don't think he has
24 a copy of it. I haven't either.

25 MR. BROWN: Yes.

Q. If I could direct your



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attention, Mr. Cimbura, to the bottom of page 3,
a question is put to you:

"Q. Well, perhaps I will put
it this way: The tissues of the
body were they badly decomposed
or what can you tell us generally
about it?"

At the top of page 4:

"A. Well yes the tissues
that I had for examination were
extremely smelly."

"Q. Yes."

"A. Which would indicate
advanced decomposition, and parts
of the heart muscle didn't look
to me certainly as a heart muscle
freshly obtained during autopsy
but there didn't appear to be that
much damage that I could see."

Then there was a question by the Court:

"What was that that didn't appear
to be...?"

And then your answer:

"A. It didn't appear to me
extensively changed. I did see,



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testimony, Mr. Cimbura?

A. Yes.

Q. And I also understand -
if you could please turn to page 10 - you were
asked whether or not Baby Lombardo had been embalmed,
and I believe your response was that she had not,
and the exchange starts right at the bottom of page
10:

"I take it this baby hadn't been
embalmed?"

"A. It has been reported to
me that the body was not embalmed."

"Q. Not embalmed?"

"A. That's right."

If I might ask you to return to
your report dated March 25th.

THE COMMISSIONER: What is that?

MR. BROWN: I'm sorry, that is
Exhibit 95C or D, I am not too sure, Mr. Commissioner.

MR. LAMEK: It is C, Mr. Commissioner.



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MR. BROWN: It will be page 2
of the report dated March 25, 1982.

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THE COMMISSIONER: March 25th,
all I have is one page. I don't know how many
pages you gave to everybody else. B has two
pages; you won't settle for B?

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What date is it?

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MR. BROWN: It is the report
dated March 25, 1982.

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THE COMMISSIONER: We will see
what is in the original.

12

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MR. LAMEK: If it is of any
help, I have two second pages. I will give you
one of mine.

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THE COMMISSIONER: There are
actually three pages?

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MR. LAMEK: Yes.

17

18

THE COMMISSIONER: So, I will
have to have it replaced sometime. I think I will
take the original. Thank you.

19

20

Have you got that, Mr. Cimbura?

21

THE WITNESS: Yes, sir.

22

MR. BROWN: Q. Do you have page
2, Mr. Cimbura?

23

A. Yes, sir.

24

25



1
2 Q. Turning to the report
3 of the results on Baby Stephanie Lombardo, separate
4 results are reported. The first one on chest
5 fluid, several others on heart tissue; one on a
6 specimen labelled "muscle".

7 Just dealing with those items,
8 Items T-52 through to Item T-59, the reports that
9 you gave were phrased that the sample was found to
10 contain a certain amount of digoxin.

11 I take it from the explanation
12 you gave to Mr. Lamek this morning, that meant that
13 with respect to the analyses that you applied on
14 those tissues, they were subjected both to RIA and
15 then also to the HPLC, with RIA conducted after the
16 HPLC; is that a correct interpretation?

17 A. That is correct, sir.

18 Q. And if I also recall in
19 the explanation that you gave to Mr. Lamek, the
20 fact that the phraseology is used; that is, that
21 the sample contained a certain amount of digoxin,
22 indicates that the results you obtained on the RIA
23 were consistent with the results you obtained on the
24 HPLC and the RIA; is that correct?

25 A. Consistent with analytical
limits, that is right, sir.



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Q. And, therefore, you only
reported the one result?

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A. That is correct.

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Q. This morning you indicated
to Mr. Lamek that you did a third a test on Baby
Lombardo, the mass spectrometry, gas chromatography,
and -- well, perhaps I can ask you, on which
specimens was that particular test conducted.

9

10

11

And, for your assistance I might
point out, if you could take your testimony again
in Volume 32 before the preliminary inquiry and
turn to page 24.

12

13

A. Yes, sir.

14

Q. The first question that
is indicated on the page is:

15

16

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"Q. So, you subjected the
Lombardo tissues and fluid to
three tests?"

18

19

20

"A. That is correct. Well,
some of them, the ones that I
mentioned; the heart, parts of the
heart and the chest fluids."

21

22

23

Would I then be correct in saying
it was the chest fluid and part of the heart tissue
that you subjected to the mass spectrometry analysis

24

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on Baby Lombardo?

3

A. That is correct, sir.

4

Q. And if you could refer

5

to page 2 of your report of March 25th. Would you

6

be able to tell us precisely which one of those

7

samples you used for the mass spectrometry test?

8

A. On page 2?

9

Q. Yes, on page 2 of your

10

report.

11

A. Well, I need a little bit

12

more detailed information to do that, and I have

13

prepared it beforehand. May I --

14

THE COMMISSIONER: Oh, yes, if

15

you can answer that.

16

A. This was T-52.

17

MR. BROWN: Q. That would be

18

the chest fluid?

19

A. That is right. Then,

20

a mixture of T-52, chest fluid, T-53, septal from
the heart, and T-54, left ventricle from the heart.

21

Q. So, in effect, there were

22

two different samples upon which you ran it; one of
them was strictly chest fluid and the second was a
combination of fluid and tissue?

23

A. That is right, sir.

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Q. And how many times would you have analyzed those specimens using the mass spectrometry?

A. As you said, there were tests.

Q. Perhaps my question was unclear. For each one of those samples, for example the chest fluid, would that have been subjected to the mass spectrometry test once or twice?

A. I don't have that detail with me now. It is probably available somewhere in the chart. I don't recall that.

Q. Very well.

I recall this morning, Mr.

Cimbura - and, again, perhaps if I go to that, when you first appeared before the Inquiry, you were asked a question, I believe, on the Lombardo child, although the name "Lombardo" is not used. You indicated that the results that you obtained from the mass spectrometry tests were not included in official report; is that correct?



EE/BB/ak

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3 A. What I meant to imply is that
4 the conclusion from that test was not included -
5 I'm sorry, the conclusion from the test was included
6 in my report saying that the substance was digoxin.
7 The conclusion of a mass spectrometry test is
8 supportive information to the other tests that the
9 substance that is being analyzed is digoxin. So,
10 I have not specified the three different tests, that's
11 right, but I concluded that the substance was digoxin
12 and so you viewed the mass spectrometry results as a
13 confirmation of a positive finding of digoxin in
14 this instance.

15 Q. In the Lombardo tissues.

16 A. That's right, sir.

17 Q. And when you perform the
18 mass spectrometry test, aside from being able to
19 identify digoxin in a sample, are you also able to
20 quantify the amount of digoxin present in the sample?

21 A. No. Well, at the time when
22 we were doing this test we were not even attempting
23 to do that because we had enough difficulty to
24 just do it qualitatively; in other words, to just
25 identify digoxin. Even that was analytically quite
a problem and I think it would be very difficult
with body tissues to do that quantitatively, at



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3 least with the equipment that we had available at
4 the time.

5 Q. And if I recall this morning,
6 Mr. Cimbura, and also when you testified on the
7 previous occasion before this Inquiry, you indicated
8 that mass spectrometry was not used in a routine
9 fashion because there were certain difficulties with
10 applying this test to a large number of samples.

11 A. Yes.

12 Q. But nonetheless is it your
13 opinion that having applied the test to that sample
14 you obtained a positive reading for digoxin?

15 A. In the case of Lombardo this
16 was the conclusion of the mass spectrometrists who
17 conducted the examination and I of course agreed
18 with that and took it into consideration together
19 with all other results that I received in this child,
20 that's right.

21 Q. Very well. If I may then turn
22 to one of the other children that you mentioned this
23 morning, Baby Belanger. I understood your testimony
24 this morning to be that you also took some samples
25 from Baby Belanger and subjected them to the mass
spectrometry analysis, is that correct?

A. That is correct, sir.



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Q. If I may then refer you to, I believe it is the September 29 report which I assume is Exhibit 95E, I believe Baby Belanger's results - yes, they are on page 3, Mr. Cimbura.

A. Yes, sir.

Q. Your report indicates that you assayed tissues marked as liver and of muscle and again the manner in which you have phrased the results, that is, a certain amount of digoxin, suggests that you performed the RIA analysis and the HPLC and RIA analysis, is that correct?

A. That is correct, sir.

Q. And again the results which you obtained from both those procedures were sufficiently consistent that you simply reported a digoxin result, is that correct?

A. That is correct, sir.

Q. And then you subsequently ran the mass spectrometry analysis on the Belanger tissue. Could you advise me as to which of those two tissues you performed the mass spectrometry test upon?

A. The liver tissue.

Q. On the liver tissue. What was the results of the mass spectrometry analysis of



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the liver tissue?

A. There were again two different tests done. The result of the first -- may I just get some more information on that?

THE COMMISSIONER: Yes, certainly.

THE WITNESS: That's right, there were again two different tests, two separate tests done. The result of the first test was negative with a notation by the mass spectrometrists that the extract was very impure. Following that we have attempted to purify more of the extract by subjecting it to successive HPLC purification and another test was conducted by GC mass spec. The result worded by the mass spectrometrists were 'may be present', and even after this extensive purification the extract was still not an ideal extract for mass spectrometry and after discussion with the mass spectrometrists and my review of all of the results I have reached a conclusion that both results were inconclusive.

MR. BROWN: Q. Therefore the results that you would place more confidence in would be the results of your own analysis using the HPLC and the RIA.

A. Well, because of that of course there was a concern in my mind and we have devised



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another HPLC procedure.

Q. For the Belanger tissues?

A. That's right.

Q. And the results of procedure, are those results reported, are they recorded in your report of September 29th?

A. Well, the conclusion is that the substance was digoxin.

Q. So, if I can simply be clear on the procedure. You initially subjected the Belanger test to the ---

A. To the regular HPLC.

Q. --- to the regular HPLC. You then subjected them to the mass spectrometry. Those results were not sufficiently certain to allow you to draw a conclusion and you subsequently subjected the Belanger tissue to another HPLC extraction.

A. A different - well, HPLC analysis using a different column and a different mode of liquid chromatography called so-called normal mode of chromatography.

Q. And after you had extracted a substance you subjected that substance to the RIA assay?

A. That's right.



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3 Q. And the results of that final
4 test I then recorded on page 3 of your report of
5 September 29th?

6 A. Well, on my report it is
7 combined result for all the tests that we have done.

8 Q. And the terminology that you
9 used in your report of September 29th refers only
10 to digoxin. So, with respect to the identification
11 of the substance measure it was then your conclusion
12 that the substance that you measured was digoxin?

13 A. That's right. There was one
14 more test in addition to what I have described. We
15 obtained another set of regions for RIA which would
16 have a different antibody from a different manufacturer
17 and we have used that also in the analyses of the
18 liver from the child Belanger and that also gave
19 positive results and my conclusion at the end of
20 all of this work was that I was reasonably satisfied
21 that the substance is digoxin, that's right.

22 THE COMMISSIONER: Mr. Brown, what
23 do you think?

24 MR. BROWN: Oh, I am very sorry.

25 THE COMMISSIONER: No, no.

MR. BROWN: I just have two more
questions, Mr. Commissioner.



EE7

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3 THE COMMISSIONER: All right, you
4 can go ahead with those.

5 MR. BROWN: Q. Mr. Cimbura, with
6 respect to the tissues that you examined from Baby
7 Belanger, do you recall the state of the tissues
8 when they were presented to you for examination?

9 A. I don't specifically recall
10 other than knowing that we had a lot of problems
11 because of the impurities that were present after
12 extensive purification of the liver tissue. So, that
13 would suggest to me there was very advanced
14 decomposition present there. Of course another
15 complication was that the level of the concentration
16 found was relatively lower than in the case of the
17 Lombardo child.

18 Q. Yes.

19 A. And suddenly those two factors
20 have a bearing on the success, or may have a bearing
21 on the success of the mass spectrometric procedure.

22 Q. And would it be fair to say
23 then that because of the state of the tissues at
24 that time that necessitated the extensive procedures
25 which you have previously described to me?

A. Well, that they necessitated
the extensive purification procedures, that's right.



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Q. And that after those extensive purifications had been done you then reached your conclusion as to the presence of digoxin?

A. I have reached my conclusion at the end of all the work that we have done on Baby Belanger, that's right.

MR. BROWN: Thank you, Mr. Cimbura, those are all my questions.

THE COMMISSIONER: Yes, all right. Well, we will take 15 minutes.

MR. LAMEK: Just before we do, Mr. Commissioner.

THE COMMISSIONER: Yes.

MR. LAMEK: Again for scheduling purposes, could I have some idea how long counsel expect to be in the cross-examination of Mr. Cimbura?

MS. FORSTER: I expect to be 15 minutes, Mr. Commissioner.

THE COMMISSIONER: Mr. Roland?

MR. ROLAND: Well, Mr. Commissioner, I'm not sure yet. I would like to be put over until tomorrow so that some of this new material that has come out today I would like to go over it.

THE COMMISSIONER: Well, that might be reasonable. We will probably get someone else.



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MR. ROLAND: I may be short, I may be some time, I don't know. I will have a better sense later.

THE COMMISSIONER: You mean some time between 5 minutes and 24 hours, is that the case?

MR. ROLAND: Well, I would say I would be somewhere between half an hour and a couple of hours.

THE COMMISSIONER: Yes, all right. Well now, I don't know who is next. Well, I guess you are next then, Ms. Chown.

MS. CHOWN: I have no questions at the present time, Mr. Commissioner.

THE COMMISSIONER: All right. Ms. Kitley?

MS. KITLEY: 15 to 20 minutes, sir.

THE COMMISSIONER: Mr. Knazan?

MR. KNAZAN: The same.

THE COMMISSIONER: The same. Mr. Olah?

MR. OLAH: It's hard to estimate. If my friend Mr. Roland is going to be two hours I suspect he will probably cover everything that I want to ask.

THE COMMISSIONER: Well, he didn't



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promise.

MR. OLAH: Knowing his brilliance.

MR. ROLAND: Well, if I am half an hour then, Mr. Olah, you can be an hour and a half.

MR. LAMEK: I have got him pencilled in for half an hour.

THE COMMISSIONER: Well, I don't know, do you want me to go on?

MR. LAMEK: No, I think that is of sufficient help. It will be much of the day tomorrow, I would say.

THE COMMISSIONER: Much of the day I think will be occupied tomorrow. Have you anyone standing in the wings?

MR. LAMEK: No, I don't and if we are going to be much of the day tomorrow then with your permission, sir, I won't arrange to have someone standing in the wings tomorrow.

THE COMMISSIONER: Well, I take it you are assuming my permission, are you?

MR. LAMEK: No, I'm not assuming it, I am asking for it.

THE COMMISSIONER: I see. Well, we will think about it.

---Short recess.



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--- Upon resuming:

THE COMMISSIONER: Yes, Miss Forster?

CROSS-EXAMINATION BY MS. FORSTER:

Q Mr. Cimbura, I would first like to turn to the note that you have on page 4 at the end of your findings on Justin Cook.

THE COMMISSIONER: Page 4 of 95A, is it?

MS. FORSTER: Yes.

Q Note 4 says:

"The concentration of digoxin in the lung T43 is above the range of values found (literature reports and research at the Centre in persons on digoxin therapy 3.4 to 30 nanograms per gram)".

Mr. Cimbura, the range that you have there, 3.4 to 30 nanograms per gram seems to correspond to the study you did which was found on page 19 of Exhibit 213?

A. That is correct.

Q And are those figures in fact based on that study?

A. At that time those figures were based on that study because as I recall it at that time I didn't have any literature reports on lung tissue.



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Q. That is what I am getting at.

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It is not really based on literature reports. It is
4 based on the study found at page 19.

4

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A. At that time it was based on
6 both but the results are ours, that is right. There
7 was no literature.

7

Q. There were no literature reports?

8

A. As I recall it.

9

Q. So your range was based on your
10 study?

10

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A. At that time, that is right.

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Q. All right. And your study
13 consisted of four samples, is that right?

13

A. That is correct.

14

THE COMMISSIONER: Please, I am not
15 numbered the way you are.

16

MS. FORSTER: Sorry, Mr. Commissioner.

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THE COMMISSIONER: It is 213?

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MS. FORSTER: Exhibit 213.

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THE COMMISSIONER: Yes.

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MS. FORSTER: The study that is found
21 at page 19 which is entitled "Digoxin Concentrations
22 in Postmortem Lung Tissue and Blood of Four Control
23 Children".

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THE COMMISSIONER: That is page 19?

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MS. FORSTER: Yes. It is the sixth page from the end, Mr. Commissioner.

THE COMMISSIONER: Yes. All right, thank you.

THE WITNESS: Or if I may qualify my answer, whatever literature reports there were they would be within this range?

MS. FORSTER: Q. Can you tell me now of any literature reports that you were relying on in giving that range?

A. Which range, the one given at that time?

Q. Yes.

A. I am trying to recall what I meant there with my note. My note or the results of our research done at the Centre were 3.4 to 30. I am not sure at this time whether there may have been some literature reports that were within this range.

Q. All right.

A. There were none that were above that range at this time. They appear to be some now which are above that range.

Q. Mr. Cimbura, if you were relying on any literature would you have notes on what you



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were relying on in making that note?

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A. Yes. I probably have them

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somewhere.

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Q. Would you mind looking through

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your notes this evening and advising me tomorrow if

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in fact you were relying on literature reports when

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you put that range down in note form? Would that be possible?

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A. I will be glad to do that. I

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am just wondering if I am missing perhaps the

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significance of your question.

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THE COMMISSIONER: I think the question

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is whether - you see you say literature reports and

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research at the Centre. We have got the research at the Centre which is on page 19.

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THE WITNESS: That is correct.

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THE COMMISSIONER: Are there other

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literature reports as well? That is all the question

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is. If there is any literature that gives you that?

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Yes?

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MR. ROLAND: Yes. I don't want to

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interrupt my friend but it would be useful for us

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perhaps to know if Mr. Cimbura does know today what

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literature he is aware of today that confirms that

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for both the lung range and as well in Note 3 he

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gives - he again refers to the literature in the heart muscle range, and then later on in respect to, I think it is in respect to the liver he talks, on page 7, he talks about the reported range there, and it would be useful to all of us I think if Mr. Cimbura does have that information today if he could tell us what literature he is referring to?

MR. HUNT: Where on page 7?

MR. ROLAND: About half way down page 7.

THE COMMISSIONER: Half way down page 7?

MR. ROLAND: Yes. Note 2 about half way down, "reported to range between ... ", I presume he is referring to some literature. If he is not, then that is my mistake.

THE WITNESS: If I am reporting it as reported I am referring to literature, that is right.

You know I will be pleased to do that. I am not sure I will be able to find it all this evening because there is a mass of literature.

MS. FORSTER: Q. Well, if you could do what you can, Mr. Cimbura, it would be appreciated.

I would next like to ask you about the study you did which is found on the sixth page of Exhibit 213.

A. On which page? Sorry.



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Q. It is on the sixth page and it is entitled "RIA Intraassay Precision Heart Tissue".

Mr. Cimbura, as I understand it one of the purposes in conducting --

A. I am sorry, I still have not located it. Which one is it again, please?

Q. It is entitled "RIA Intra-assay Precision Heart Tissue". It is found on the sixth page of Exhibit 213.

A. Okay. Sorry, I have it now. Yes.

Q. As I understand it one of your purposes in conducting the study was to attempt to provide a range of digoxin levels that you would expect to find in the heart tissue of children who had been on digoxin therapy; is that correct?

A. That is right.

Q. I understand that the tissue from only two children was studied?

A. For this particular purpose here.

Q. Right.

A. Because the main purpose for this one was to study the intraassay variation in the recovery.

Q. Right.

A. Or the second purpose or more



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extensive purpose that took more children to study
was to get a range of values.

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Q. All right. And Samples No. 1 and
No. 2 pertained to the same child, did they not?

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A. That is right.

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Q. Would you agree with me there
is quite a difference in the results you obtained
between one child and No. 3?

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A. That is right.

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Q. And are you able to explain that
difference, sir?

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A. Well, that is the purpose why,
you know, I have conducted this study because as a
forensic toxicologist I know there is always a
variation in the concentrations of different subjects
under therapeutic conditions. This is a well known
fact of forensic toxicologists, so in an attempt - you
would expect to find variation but you don't know
the extent of the variation.

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Q. Did it surprise you in any way
that the variation was - I think it went from 41.9 to
414? Did that kind of variation surprise you?

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A. The results were of course
interesting to me but I don't think particularly
surprising. I expected to find a range.



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Q. All right. And have you seen this type of range in other types of studies you have conducted as a toxicologist?

A. With other drugs you mean?

Q. Yes.

A. I am just trying to recall some of the drugs. Of course with other drugs we usually don't study heart.

Q. Yes.

A. The reason we studied heart is because the heart were the specimens we had only from some children in the investigation so that with other drugs we would not normally study heart variations. We would study or be familiar with let's say blood variations and, well, I guess the simplest is alcohol. Well, maybe alcohol wouldn't be a good example because it is not a medicine or a drug.

Q. In your studies of any other kind of drugs have you come across ranges that were that large? Is that out of the ordinary or is that something that you find in other situations?

A. No, I expected to find wide ranges.

Q. Now dealing with your tests on tissue for a moment, when Dr. Ellis gave his evidence

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he indicated that he had some major misgivings about using the RIA procedure to determine the digoxin level in tissue.

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Is that an opinion you would share with Dr. Ellis?

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MR. HUNT: I am sorry, what page is that on?

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MS. FORSTER: I don't have Dr. Ellis' transcript with me.

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MR. HUNT: I would appreciate knowing --

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MS. FORSTER: Perhaps I could look it over the --

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MR. HUNT: My position is if other evidence is going to be put to the witness I want to know the page, where it is, so that I can see what the evidence is.

16

17

MS. FORSTER: All right. Maybe I will just rephrase my question.

18

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Q. Do you have any major misgivings about applying the RIA procedure in conducting digoxin tests on postmortem tissue?

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A. Well, I am not sure if I would call them misgivings. I know the advantages and disadvantages. I am familiar. That is my job as a forensic toxicologist.



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One of the disadvantages of the RIA procedure is that it may cross-react, the antibody may cross-react with some other related substances.

Q. And I believe that is one of the misgivings you mentioned last time you were here.

Have you read your evidence from the last time you were giving evidence here before you came today? Did you re-read the evidence you gave?

A. Yes I recall reading it right some time after, briefly, yes.

Q. Do any other misgivings come to mind other than those you told us about last time?

A. Misgivings about that method?

Q. Yes.

A. Is that what you are referring to?

Q. Yes.

A. As I said I would not call them misgivings. They are disadvantages.

Q. Disadvantages then.

A. I would say that is a major disadvantage.

Q. Then, sir, you did - one of the tests you did on the cross-reactivity of the RIA procedure is found on the tenth page of Exhibit 213. It is entitled "RIA Cross-Reactivity".



FF.11

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A. I am sorry, I don't have a number.

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Q. It is the page just before the

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graph.

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A. Yes, I have it.

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Q. I was a little unclear as to

7

your procedure in this particular test. Did you run
each of these drugs through the RIA procedure to

8

determine whether or not you got a reading for digoxin?

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Is that how it was done?

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A. That is right.

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Q. All right. So the test then

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doesn't tell us whether these drugs react in the body
such as to affect the digoxin level in blood?

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A. Well, some exception to that is

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the blood obtained from a child who was on

15

spironolactone therapy.

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Q. Right. Now with the exception of

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that one the rest, for example, the child on morphine,

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this test doesn't tell us whether or not the morphine

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might react in the body such as to affect the digoxin

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level you got on the RIA test, does it?

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A. If I understand you correctly,

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it does not, that is right.

23

Q. Right.

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A. The other substances were run

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FF.12

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as pure solutions, that is right.

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Q And turning to the next, Doctor,
where you did a test on the stability of digoxin in
Klotz solution, how many samples of Klotz solution
did you use in this test?

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A Initially we spiked one sample
which was divided into two portions, as I recall it.
One kept at refrigeration and one kept at room
temperature.

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Q Yes.

A Subsequently a small portion, a
big portion was analyzed on different occasions.

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Q And did it all come from the
same initial Klotz solution?

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A That is right.

Q And I take it from the evidence
you gave at the preliminary hearing that different
solutions of Klotz solution may have different make-ups;
is that correct?

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A In a sense, yes. I believe what
I was referring to then was the Klotz solutions that
were received surrounding the specimens of tissue
from the various children; in my experience we have
tested them for some components. The composition
or the components of the Klotz solution varied, that
is right.



FF.13

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Q. And I take it because of that
had you used a different solution of Klotz solution,
the results in this particular test may have been
somewhat different?

A. Well, this was done as I recall
it on Klotz solution that we made ourselves in my
laboratory according to the protocols supplied to us
by the Hospital.

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Q. All right. What was the protocol designed to do?

A. Well, the protocol, by protocol, I mean the concentration of the various components to make that solution.

Q. Is it your understanding that the Hospital Klotz solution is made according to a recipe, so to speak?

A. So to speak, that's right, yes. All solutions are made of so-called, so to speak, recipes, that's right.

Q. Now, dealing with the test, that is the second page after the graph:

"Comparative analysis of 'fresh' and Klotz-fixed heart and lung tissues."

A. Yes.

Q. When you listed values in the "fresh" specimens and the Klotz-fixed specimens, for example, in Case 1, you have a value of 383 and then a value of 6.7.

Is that a reading of digoxin or digoxinlike substances?

A. That is by RIA, that is digoxin and digoxinlike substances.

Q. And similarly is that the



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case on the next study on page 14, dealing with the tissue from "control children on digoxin therapy" in regions of the heart?

A. Yes. That is analyzed by RIA, as the No. 1 asterisk says, that's right.

Q. Now, you indicate on this study that the storage of the tissues ranged between one and two months.

A. That's right.

Q. Did you make any attempt at all to measure your results in terms of the exact storage time?

A. Well, this particular experiment was done in my laboratory.

I am not sure if I understand your question.

Q. For example, in Case No. 11, you had a result of 10.3, in Case No. 9, you have a result of 1.9. We know they were both stored for somewhere between one and two months.

Did you, in your study, determine whether or not the length of the storage time was significant such that it would lead to different results?

A. Well, from the previous



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material that you questioned me on, the graph illustrates that the time may be significant, yes.

Q. That is exactly what I am getting at, Mr. Cimbura, because it seems that, on the graph, the peak comes at about 50 days.

A. Yes.

Q. In between the one and two month period, and I would have thought that, in conducting your study, if the storage time is one to two months, the exact time might be rather critical. Did you take that into account in doing this study?

A. Well, I'm sure I considered this factor. I am not sure if you are implying why we are not studying them longer than that?

Q. No. I want to know whether or not -- I assume, when you got these results, you knew, because you put in a range of one to two months, you knew how long each of your case numbers was stored. But did you take into account, in arriving at your results, that some of them may have been stored around this 50-day period and, thus, been elevated?

A. What was elevated?



Cimbura
cr.ex. (Forster)

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Q. Well, let me try it
this way. For Case No. 11, you have a value of
10.3.

A. In the fixed heart
region.

Q. Right. And that is
after storage in Klotx Solution.

A. That is why I put a
period between one to two months.

Q. Let's suppose for a
moment that it was stored in Klotz Solution for
50 days.

A. That is approximately
two months.

Q. Yes, just under two
months. That would put it on your graph at a
peak period, so that we would get a higher result
than had it been stored for 30 days or 60 days,
if your graph is correct.

A. Well, there is a possi-
bility of that, that's right.

Q. Now, all I am asking is
was that taken into account by you in arriving at
these results?

THE COMMISSIONER: 50 days, because



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50 days is right in the middle of the zero to 60 days, is that it?

MS. FORSTER: Yes, sir.

THE COMMISSIONER: There is some kind of a comparison if you go back to the page before, because, apparently on the chart, on page 13, they are all between six and nine months and, on page 14, all between one and two months; so there is some kind of comparison there.

Have I got this right? Period of storage in the comparative analysis on page 13 is six to nine months, and the comparative analysis on page 14 is one to two months; is that right?

Have I got this? Is that why you separated these two? One, we have got hearts and we have the second region of hearts too but, for some reason, there happens to be a shorter storage period in the region of hearts than there was in the hearts themselves.

Mr. Cimbura, do you --

THE WITNESS: I'm sorry?

THE COMMISSIONER: Would you look at page 13, at page 14.

THE WITNESS: I don't have the number, sir.



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THE COMMISSIONER: No, I didn't have mine either. What I am trying to say is that, for some reason, you are comparing the comparative analysis with hearts, the period, the approximate period of storage is six to nine months. When you are doing the region of hearts, for some reason, the period of storage was one to two months.

Was that deliberate or did that just happen?

THE WITNESS: No, that just happened.

THE COMMISSIONER: It just happened, I see.

THE WITNESS: In this study, the hearts were in the Hospital.

THE COMMISSIONER: Yes.

THE WITNESS: From the beginning.

THE COMMISSIONER: You are looking at page 13, yes.

THE WITNESS: And at some later time, I had the idea I should get those hearts back and go back to them.

THE COMMISSIONER: All right.

THE WITNESS: And I had them at approximately these periods of time.



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GG7

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THE COMMISSIONER: Yes. I see.

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THE WITNESS: The other experiment,

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we started that ourselves in the laboratory, but I

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believe that we were pressed in time to get some

6

results, so we concluded in this period of time.

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THE COMMISSIONER: Thank you. I

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just mentioned that, Miss Forster, because it may be

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of some assistance to you. I don't know that it is.

10

MS. FORSTER: Yes. Thank you, sir.

11

Q. Mr. Cimbura, I would

like to turn to your report now.

12

Dealing with the first page of

the report dated January 11, 1982 --

13

A. Yes.

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Q. -- the samples on the

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first page for Justin Cook, those were fresh

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samples?

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A. Well, the first three.

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Q. The first three.

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A. Up to T-43.

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Q. And T-43 was a fresh

sample of lung, and you found a reading of 153
nanograms?

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A. That is correct.

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Q. And if we turn to the

next page, T-11, the samples of heart and lung in

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T-11 were samples stored in Klotz solution?

A. Those were fixed in Klotz solution, that's right, after some period of time.

Q. Do you recall the period of time?

A. I don't recall it now. That information is somewhere.

Q. I think you indicated at the Preliminary that it was three to five months. Does that sound about right to you?

A. Well, if I indicated that at the Preliminary, then I have done some estimation.

Q. You found a value for the lung of 32 nanograms of digoxin and digoxinlike substances?

A. That is correct.

Q. And what is your explanation for the level going down from 153 nanograms in fresh tissue to 32 nanograms in the tissue in Klotz solution?

A. My explanation for that is the results of the research you just asked me to examine. In other words, two factors are involved;



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the chemical degradation of the drug as well as
diffusion of the drug from the heart into the
surrounding tissues - I'm sorry, surrounding
Klotz solution.

Q. In T-42, sir, you
got a result of 1,177 nanograms in the heart
muscle.

A. That is correct.

Q. And testing it, after
Klotz solution, the values you had for the heart
are anywhere from 36 to 39 nanograms?

A. That is correct.

Q. Do you explain that
reduction on the same basis?

A. That is correct. In
other words, degradation and diffusion, that's right.

Q. Does that not strike you
as a large difference?

A. Yes. It is a large
decrease, yes.

Q. And are you satisfied,
based on the research that you have done, that that
is the kind of degradation one should see if it has
been stored in Klotz solution for three to five
months?



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A. Well, in general

principle, by research I was able to conclude that there is a diffusion process and degradation which would be expected to result in a decrease, and the decrease could vary based on a number of variables.

Q. It seems to me that the decrease in the lung sample is far, far smaller than it is in the heart sample.

A. That is right.

Q. Does that cause you any concern?

A. Well, the concern would not be, I suppose, the right word for me, but it indicates that, in lung tissue on this patient, this one sample, it declined maybe less, and one possible explanation for that might be that diffusion, for example, is a process which is dependent upon the concentration. So that the higher concentration you have to begin with, the greater diffusion you are going to have.

Q. Have you been able to quantify that?

A. Well, diffusion is well defined in chemical and scientific literature.

Q. Have you been able to quantify



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the relationship between the diffusion and the concentration in the initial fresh tissue?

A. The graph which has been presented illustrates the extent of degradation or possible extent of degradation. It works from initially high concentrations and you end up with lower concentrations.

Q. But this graph only goes so far as to tell us an initial concentration of 550 nanograms after roughly seven months decreases to approximately 100 nanograms. It doesn't explain a reduction of 1,100 to some 39.

A. Well then, there is the second part there, which is the diffusion. The diffusion is also illustrated in the document, I believe it is 13 and 14. By mere observation, the Klotz solution contains the digoxin. The only way that digoxinlike substance could have come to the Klotz solution, it must have diffused from the heart into the surrounding solution; that is the only way it could have come there.

Q. Are you satisfied that a combination of the diffusion and the results you got that are shown by the graph account for this substantial reduction from 1,100 to 39?



GG12 2

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A. In my research, I observed a very wide decline, depending on many, many factors. It ranges from in some cases where it is relatively small and some where it is very, very dramatic.

MS. FORSTER: Mr. Commissioner, I expect to be another ten or fifteen minutes. Do you wish me to continue?

THE COMMISSIONER: How do you feel, yourself?

MS. FORSTER: I'm quite happy to continue, if it is all right with you.



Cimbura, cr.ex.
(Forster)

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BB/cr

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THE COMMISSIONER: Well, if you really think it is 10 minutes. Are you inclined to be honest when you say that?

MS. FORSTER: Never.

THE COMMISSIONER: Well, we will let you go to a quarter to five.

MS. FORSTER: Very well.

THE COMMISSIONER: If you don't finish then we will put you over, as they say.

MS. FORSTER: Fine.

Q. Next, Mr. Cimbura, dealing with your tests on the Pacsai baby your initial ones are summarized in your report of January 11th and then I take it you did further studies that are shown in your report of March 25th on page 2.

A. And also September 29th.

Q. That's right. I would like to deal with the studies that you did that are shown on page 2 of your March report, Samples T-49, T-51.

A. T-49, T-50 and T-51?

Q. That's right. Have you got those?

A. Yes.

Q. Are you aware, sir, that Dr. Ellis also tested for digoxin levels on those



Cimbura, cr.ex.
(Forster)

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three samples?

A. Not specifically as far as
I can recall.

Q. Mr. Registrar, I wonder if
the witness could be given Exhibit 210, please.

THE COMMISSIONER: I'm sorry, what page
did you say?

MS. FORSTER: Of the digoxin kit book.
It is page 171, Mr. Commissioner, and I am also referring
to page 2 of the March 25th Cimbura report.

THE COMMISSIONER: Yes, all right.

MS. FORSTER: Mr. Cimbura, if you
could turn to page 171 of that exhibit, which is
near the back.

A. Yes.

Q. These are results that Dr.
Ellis got when he tested these samples, among others,
and firstly No. 5 is 1287/81 when he says that's a
sample of the miocardium and that he got a result of
greater than 5. That same sample number shows up on
your T-51.

A. Well, if it is the same, yes.
I am assuming it is the same.

Q. They are both marked 1287/81
Pacsai miocardium?



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A. Yes.

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Q. And you get a result of 21
nanograms?

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A. Yes.

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Q. So, Dr. Ellis' result is at
least consistent with your result. Do you agree?

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THE COMMISSIONER: I can't remember
now. This was not the one that Dr. Ellis disowned,
was it. He disowned certainly the earlier one but
did he disown this one?

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MS. FORSTER: Yes, as I recall, sir,
the first tests he did show up in 32B and they are
all greater than two.

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THE COMMISSIONER: But these are the
ones that he didn't report to anyone. Did he say
that he did?

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MS. FORSTER: This is his private
work. I think he has virtually disowned all the
tissue samples.

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THE COMMISSIONER: Yes. Well, all
right. Well, I just want to make sure that Mr.
Cimbura, if I am right, that Dr. Ellis is not putting
these forward as his figures, is he? Was he putting
these forward as his figures?

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MR. ROLAND: Well, as I recall it, Dr.



1 Ellis put them forward as the figures he arrived at
2 but also indicated that he had very little or no
3 experience with tissue samples and because he didn't
4 think they were reliable he didn't treat them so.

5 THE COMMISSIONER: Yes, that was my
6 recollection of it for both of them, particularly the
7 first set. But this second set as well. I just
8 wanted to make sure.

9 MS. FORSTER: I think, sir, he indicated
10 that he had grave misgivings about using RIA at all
11 on tissue.

12 THE COMMISSIONER: Well, that's fine.
13 But the only thing is if you put these figures to
14 Mr. Cimbura he might take it that he is getting into
15 a row with Dr. Ellis if the figures differ, that's
16 all.

17 MS. FORSTER: My intention was to ask
18 him his opinion as to why the figures with respect
19 to one finding differ, if he could explain that.
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MR. HUNT: Then my friend is going to have to put all of the evidence that Dr. Ellis qualified as his own lack of experience.

THE COMMISSIONER: I would have thought so. I would have thought so, Ms. Forster. Maybe I'm wrong but you have to tell Mr. Cimbura if you are going to do this what he says, with respect. If you want to compare Dr. Ellis' figures and his figures because presumably Mr. Cimbura is sticking by his to the extent that he has stuck by them, whereas, Dr. Ellis was not sticking by his as I remember it. So, there you are.

You know, I don't want to stop you but I think Mr. Hunt is right, before you ask him to compare the two figures you have to say everything that Dr. Ellis said about his figures.

MS. FORSTER: Okay. It is not that important, Mr. Commissioner, I will move on.

THE COMMISSSIONER: That's one I won.

MS. FORSTER: Q. Mr. Cimbura, dealing with Kristin Inwood. The tests you did on her, which are found in your January report on page 7 and 8 and in particular Sample T26.

A. Sample which?

Q. T26.



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A. It is not on that page.

Q. On page 8.

A. Oh, I'm sorry.

Q. Okay, that was a sample of
blood. You indicate:

"No digoxin could be detected; detection
limit of 2 nanograms per millilitre."

A. That is correct.

Q. I thought you told Mr. Lamek
that your detection limit was 1 nanogram per milli-
litre. Could you explain that notation to me?

A. Yes, providing we had enough
sample the usual detection limit is 1 nanogram per
millilitre. In this instance, as I recall it, the
sample was very small and because of that we couldn't
achieve our normal detection limit.

Q. I see.

A. That's the reason why I specified
the divergence from normal.

Q. Are you satisfied, sir, that
your tests should have detected any digoxin that
was over and above that limit of 2 nanograms?

A. It should have, yes.

Q. Mr. Cimbura, one final point.
In a number of the notations you make after tests



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you have done on exhumed bodies and, just as an example, I refer you to your September report, page 2, and you are dealing with the Bilodeau baby and in your third note you discuss the embalming process and the long burial and decomposition and say that might have influenced the digoxin concentrations and, you say:

"For this reason comparison of digoxin values in the exhumed autopsy material with those of fresh autopsy tissues may not be valid. In view of this and other factors the results obtained in this case are considered inconclusive with respect to digoxin toxicity."

You used that phrase, sir, in referring to, I think just about every case in which you have examined exhumed tissue and I wonder if you could tell me what you meant by 'in view of this and other factors'. What are the other factors?

A. That's a good question. I have thought about it last night when I read my report. The thought that came to my mind is that I may have meant there in addition to that it is still only tissue level as compared to blood. I believe I mentioned previously that, you know, blood



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concentrations, like, from the point of view of forensic toxicology, concentrations in blood are more significant than concentrations in the tissue alone.

MS. FORSTER: I see. Thank you very much, Mr. Cimbura.

THE COMMISSIONER: Thank you, Ms. Forster, you turned out to be as honest as the day is long.

MS. FORSTER: Yes, I guess I turned out to be honest.

THE COMMISSIONER: Well, unless anyone has a desperate need to give one question but we will rise until 10 o'clock tomorrow morning.

---Whereupon the hearing adjourned at 4:45 p.m. until Thursday, October 20th, 1983 at 10:00 a.m.

